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RELAPSING FEVER AND OTHER SPIROCHAETOSES.

NICOLLE (Charles) & ANDERSON (Charles). Etude comparative de quelques virus récurrentes, pathogènes pour l'homme. [**Comparative Study of Relapsing Fever Viruses Pathogenic to Man.**]—*C.R. Acad. Sci.* 1927. May 23. Vol. 184. No. 21. pp. 1225–1226.

—— & —— in collaboration with RAHAL (Magid). Etude comparative de quelques virus récurrents, pathogènes pour l'homme.—*Arch. Inst. Pasteur de Tunis.* 1927. June. Vol. 16. No. 2. pp. 123–206. With 11 charts in text. [22 refs.]

The investigations described in these papers concern four viruses of the relapsing fever type, viz., the Tunisian human strain, the Spanish strain, the African tick fever strain and the naturally occurring field vole strain of Dakar, all of which are known to be inoculable to man. They have been most exhaustively studied from the point of view of behaviour in experimental animals, immunity and transmission. The longer of the two papers gives a mass of experimental evidence on which the conclusions are based. It was found that the viruses fall into three groups: (1) The Tunisian human virus which is identical with the louse borne virus of other parts of the world; (2) the Spanish virus; (3) the virus of African tick fever and that of the field vole.

C. M. Wenyon.

NICOLLE (Charles) & ANDERSON (Charles). Sur l'origine des fièvres récurrentes humaines. [**Origin of Relapsing Fevers in Man.**]—*Bull. Inst. Pasteur.* 1927. Aug. 15. Vol. 25. No. 15. pp. 657–665. [10 refs.]

For many years one of the authors has held the view that the constant origin of Tunisian louse borne epidemics of relapsing fever in districts near the Sahara would be explained by the discovery of a reservoir of the virus, probably a tick. Attempts to transmit the virus by *Ornithodorus savignyi* which might serve as a reservoir and which is common in Southern Tunis have failed. Two important facts have, however, recently come to light. These are the discovery of a tick-transmitted spirochaete in Spain and the field vole strain of spirochaete in Dakar. A third fact, which only became known after the article was written, is the occurrence of the natural gerbil strain and its transmission by *Ornithodorus normandi*. Of the numerous experiments which have

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been conducted three are mentioned here. The Spanish strain is transmissible by the louse, the naturally occurring field vole strain of Dakar is infective to human beings, while this same strain by all tests applied is closely related to that of African tick fever.

The conclusion reached by the most interesting discussion which follows is that relapsing fever spirochaetes commenced as parasites of small mammals, became adapted to human beings through the agency of ticks and finally through their close association with lice acquired the property of survival in and transmission by these insects. The evolution has passed through the following stages :—

1. An infection of small mammals transmitted by ectoparasites which are possibly, though not necessarily, species of *Ornithodorus*.
2. The intervention of ticks of the genus *Ornithodorus* which obtain the virus and conserve it and which require large mammals for the maintenance of their adult stages.
3. The intervention of human beings infected by the ticks, more as an occasional accident than as a necessity.
4. The intervention of the louse by the adaptation to it of the spirochaete which is nevertheless still transmissible by the tick.
5. The complete adaptation to the louse and the consequent spread from Africa throughout the Old World.

C. M. W.

NICOLLE (Charles). L'évolution des spirochètes et le mécanisme de la crise dans les spirochétoses. [**Development of Spirochaetes and Mechanism of Crisis in the Spirochaetoses.**]—*Arch. Inst. Pasteur de Tunis.* 1927. June. Vol. 16. No. 2. pp. 207–217. [2 refs.]

This very interesting article commences with two assertions : (1) Relapsing fever spirochaetes have two stages, the one visible and the other invisible ; (2) recovery occurs with a suddenness to which there is no parallel in other infections ; the spirochaetes which have become extraordinarily numerous in the blood disappear in a few hours.

In the louse the spirochaetes taken up from the blood disappear during the first few hours. During six days it is impossible by any means available to demonstrate the organisms. Then suddenly they become exceedingly numerous in the body fluids.

In man the same series of events occurs. There are numerous spirochaetes in the blood and at the moment when they would appear to be triumphant they become less vigorous and agile, and before their actual destruction supervenes it can be noted that they assume a new form which is longer, thicker and less mobile and which may be termed *bacillary*. In a few hours all trace of spirochaetes is lost, but nevertheless the blood remains infective for several days. When relapse occurs this is announced by a return of fever and the re-appearance of typical spirochaetes. At the commencement of the relapse there may be few spirochaetes in the blood ; yet a drop placed in sterile vaseline and incubated will in a few hours be swarming with them. Such cannot have arisen except from pre-existent invisible forms. As regards the virulence of the visible and invisible forms it has been shown that the fluids of the louse are most likely to infect shortly before spirochaetes re-appear. The invisible forms are thus most virulent at this particular stage. The evidence regarding the invisible forms in man is less certain, though if the infectivity of the blood when spirochaetes are not present be due to such, it is reasonable

to assume that invisible forms are present even when spirochaetes are numerous. The Spanish relapsing fever strain in the gerbil (*Meriones shawi*) gives rise to an infection without visible spirochaetes. Yet the merest trace of its blood will infect a guineapig, even by way of the conjunctiva, which allows of the passage of only an infinitesimal number of organisms.

There are thus three stages of the spirochaete—indifferent granules, previsible and infective forms, and the adult spirochaete in which arises once again the ancestral type, a saprophyte.

The capacity of the invisible forms to develop into spirochaetes varies in different experimental animals as also in the invertebrate hosts. Thus though the Spanish relapsing fever strain can be transmitted by the louse, spirochaetes never appear in these insects as they do in the ordinary relapsing fever strain.

The crisis in relapsing fever is thus to be regarded as the breaking up into invisible forms of the saprophytic spirochaetes under the influence of antibodies and the regrowth of these to the infective previsible forms and finally to the spirochaetes again. If there is defective antibody production, then there is a tendency for the saprophytic spirochaete to reproduce indefinitely and bring about destruction of the host by the sheer mass of organisms present. It is suggested that a similar conception may explain the behaviour of other organisms such as the pneumococcus.

C. M. W.

NICOLLE (Charles) & ANDERSON (Charles). D'une erreur commune dans la conduite des expériences portant sur la détermination des agents de transmission des spirochétoses et de la même erreur dans toutes les investigations analogues. [**Common Error in the Interpretation of Experiments on the Transmission of Spirochaetoses.**] —*Arch. Inst. Pasteur de Tunis.* 1927. Sept. Vol. 16. No. 3. pp. 228–232.

The article is written with the intention of emphasizing the warning already hinted at in another paper, namely, that it is fallacious to conclude that, because the inoculation to an animal of the products obtained by crushing an insect or other invertebrate which has previously ingested infective material produces infection, the insect or other invertebrate is capable of transmitting the virus in nature. In the case of the louse, which transmits relapsing fever by the escape of infective fluid from its body when damaged, it might be urged that the experiments objected to have been regarded as sufficient. But in this case it has been demonstrated that a person may be bitten by many thousands of infective lice without acquiring an infection, while the contamination of the slightest wound or the conjunctiva with the smallest quantity of fluid from such a louse will produce infection. Furthermore it has been shown that on the body it is the custom for lice to be damaged by crushing or the severance of a leg which permits of escape of fluid on to the skin. The mere injection of the fluid of crushed lice into animals would have been insufficient to incriminate the louse as a vector. In the case of ticks the infection produced by the unnatural method of injection of such fluid has frequently been regarded as proof that a vector is being dealt with, and the authors very rightly protest against these fallacious deductions. [The reviewer is

in entire agreement with these views, and has on several occasions pointed out in this *Bulletin* that the sand fly cannot, as a result of such inoculation experiments, be regarded finally as the vector of leishmaniasis till the natural method of infection has been elucidated, though the association of the fly with the disease and the particular type of development of the leishmania in the fly render it highly probable that it is the vector].

C. M. W.

ROSENHOLZ (H. P.) & GILBERT (M. J.). Weitere Untersuchungen über die Rolle der Wanzen in der Epidemiologie des Rückfallfiebers. [**Further on the Rôle of Bugs in the Epidemiology of Relapsing Fever.**]—*Cent. f. Bakt.* I. Abt. Orig. 1927. Sept. 10. Vol. 103. No. 6-8. pp. 348–353. [3 refs.] [Microb. Inst., Educ. Commissariat, R.S.F.S.R., Moscow.]

Experiments on the behaviour of relapsing fever spirochaetes in bed bugs have already been described by the first author (this *Bulletin*, Vol. 24, p. 685). In the present paper further results are recorded. Attempts were made to infect mice by injecting them with crushed eggs or larvae resulting from adult bugs harbouring spirochaetes. In no case did infection occur. Similarly further attempts to transmit the spirochaetes by the bite of infected bugs gave only negative results. In this experiment the mice and bugs were kept together at 37° C., so that each mouse was bitten many times. The effect of low temperatures (+5° to —20° C.) was tested on infected bugs and it was found that though the bugs died at the lower temperature the spirochaetes in them did not lose their motility. Similarly the spirochaetes in the bugs were not seriously influenced by starvation. A 78 days' fast on the part of the bug did not influence the vitality or virulence of the spirochaetes. In certain starved bugs extraordinarily long fine regularly coiled motionless spirochaetes occurred and these did not regain their motility when the bugs were allowed to feed. The method of inoculating spirochaetes into the body cavity of bugs suggested the similar inoculation of other organisms with a view of testing their survival. The organism of rat bite fever could be demonstrated in the body fluid for 2 days, while *S. pallida*, *S. cuniculi* and *S. icterogenes* (*S. icterohaemorrhagiae*) survived only a few hours. Trypanosomes (*T. equiperdum*) could be recovered up to the 8th day. The previously recorded infections of bugs with relapsing fever spirochaetes were brought about by allowing bugs to feed on experimental animals. It is now shown that the same result is obtained by allowing bugs to feed on human beings suffering from relapsing fever. Immediately after the ingestion of spirochaetes these organisms appear in the body cavity fluid of the bugs and they persist there for the length of the observation (46 days). A drop of body cavity fluid at the end of 46 days produced infection in a general paralytic. It was noted that, if a bug became infected after feeding on a human being, the spirochaetes in its body fluid were reduced in number if the bug were given its next feed on mouse blood. The original number was regained only after 4 or 5 feeds, showing a gradual adaptation of the human spirochaetes to substances in the mouse blood.

C. M. W.

MACKIE (A. S.). **Relapsing Fever in Meru.**—*Kenya & East African Med. Jl.* 1927. July. Vol. 4. No. 4. pp. 121–122.

Relapsing fever, transmitted by ticks, is of common occurrence in Meru in Kenya. All the cases seen, except two, were in natives. The onset is sudden with headache, fever and generalized pains. Frontal headache is the chief symptom complained of. Enlargement of the liver or spleen, jaundice or bronchitis did not occur. On admission the temperature usually varied between 102° and 103° F. When N.A.B. is given the temperature falls to normal or subnormal on the 2nd, 3rd or 4th day. Spirochaetes are easily found in stained films and are numerous. It was not possible to follow the majority of cases, but one, a Somali syce, had four relapses, the longest interval being 28 days and the shortest 16 days. The habits of the tick vary, for in the North Frontier Province they live in the sand under acacia trees and attack as readily by day as by night, while in the Meru Reserve they occur mainly in the huts of the natives and probably bite only by night. In the native the bite is not followed by any local reaction, but the reverse is the case with the European.

C. M. W.

i. MATHIS (C.), DURIEUX (C.) & EWSTIFEIEF (C.). Nouveau cas de fièvre récurrente contractée à Dakar. [**Relapsing Fever at Dakar.**] —*Bull. Soc. Path. Exot.* 1927. May 11. Vol. 20. No. 5. pp. 441–445. [7 refs.]

ii. ——. Foyer endémique de typhus récurrent à Dakar.—*Ibid.* July 13. Vol. 20. No. 7. pp. 700–704. [6 refs.] [Pasteur Inst., Dakar.]

i. The first paper reports a case of relapsing fever at Dakar. It is the second in which the infection undoubtedly occurred in this town. The first case was noted recently by GUILLET (this *Bulletin*, Vol. 24, p. 688). The spirochaetes were isolated from the first case in mice, but the strain was unfortunately lost. From the second case the strain was isolated also and has been maintained easily in mice, in which it behaves like the organism of tick fever rather than that of the louse borne disease. The absence of ornithodorus at Dakar suggests some other vector, and the possibility of the spirochaete being that of the field vole—*Spirochaeta crocidurae.*

ii. The second paper records three further cases. Two of these were in natives who occupied one room. The first case did not reveal any spirochaetes on direct blood examination but the blood produced infection in mice. In the blood of the second case very rare spirochaetes were found and mice were again infected. The third case was also in a native, who was found comatose and moribund in the street. Blood examination revealed fairly numerous spirochaetes. The temperature was 39·6° C., there was a generalized jaundice and the urine contained much bile. The patient died without recovery of consciousness. At autopsy the liver, spleen and kidneys were congested, but without degenerative lesions. The bases of the lungs were likewise much congested while the stomach mucosa showed haemorrhagic spots. Mice inoculated with the patient's blood became infected, as also one of two mice inoculated with the products obtained from crushing four lice collected from the patient.

There appears to be no doubt that the three cases were of Dakar origin. As regards the spirochaetes isolated in mice they are readily handed on from mouse to mouse and in this respect resemble *S. crocidurae.* It is evident that at Dakar there is an endemic focus of relapsing fever.

C. M. W.

AZNAR (Pedro). Algunas investigaciones clínicas y experimentales sobre la fiebre recurrente española. [**Clinical and Experimental Study of Spanish Relapsing Fever.**]—*Arch. Inst. Nac. Higiene de Alfonso XIII.* 1926. Oct. Vol. 4. No. 4. pp. 121–127. [16 refs.]

The author states that during an antimalaria campaign conducted in August, September and October, 1925 at Fuenteovejuna (Cordoba, Spain) four relapsing fever cases were seen which resembled clinically those described by de BUEN and others. Towards the end of 1924 certain experiments were commenced with a strain of spirochaete isolated from a human being by inoculation of a guineapig. The strain was readily passed from guineapig to guineapig as also to rats and mice. Certain cultural experiments were also successfully carried out. Various rats and mice which had recovered from a spirochaetal infection five months before were inoculated with either *Trypanosoma gambiense* or *T. brucei.* Two or three days later spirochaetes reappeared in the blood of all the mice and in some they persisted for one or two days after trypanosomes had appeared in the blood. This observation is in accord with those of various authors who have noted that after apparent recovery of animals the virus may still persist. [A similar observation was made by the reviewer who noted the reappearance of spirochaetes in a mouse inoculated with *Trypanosoma cruzi* (WENYON's *Protozoology,* Vol. 2, p. 1256).]

C. M. W.

DE BUEN (Sadi). Estado actual de nuestros conocimientos sobre la fiebre recurrente española. [**Existing Knowledge of Spanish Relapsing Fever.**]—*Arch. Inst. Nac. Higiene de Alfonso XIII.* 1926. Oct. Vol. 4. No. 4. pp. 143–156. With 2 text figs. [11 refs.]

The paper describes relapsing fever in Spain with special reference to its transmission by the tick, *Ornithodorus marocanus,* which frequents pig stys and appears to nourish itself on the pigs. The information is much the same as that contained in two papers previously reviewed (this *Bulletin,* Vol. 23, p. 590) but some new facts are brought forward. Mention is made of certain experiments by ORTEGA, who has demonstrated the infectivity of young ticks bred from infected adults. In the present paper the author gives the name of the spirochaete as *Treponema hispanicum* n. sp., though it had already been given in this form in the second of the two previous papers referred to above, and in the same form without the n. sp. in the first. The new name undoubtedly dates from the first paper.

Reference is again made to the attempts to infect pigs by inoculation of crushed ticks. These were not successful [as erroneously stated by the reviewer in his summary of the previous papers].

C. M. W.

HÖGLUND (Gustaf). Studien ueber die Blutveränderungen bei Febris recurrens africanus (Impfrekurrens). [**Blood Changes in African Relapsing Fever induced Therapeutically.**]—*Acta Med. Scandinavica.* 1927. Vol. 67. No. 1–2. pp. 105–165. With 1 folding diagram. [21 refs.] [" Karolinska " Inst., Stockholm.]

A very exhaustive examination of the blood in 29 cases of induced relapsing fever gave the following results: As a rule spirochaetes (*Treponema duttoni*) can be demonstrated in the blood by direct microscopical examination. Occasionally during the course of an attack an unusual type of organism appeared. This was shorter and thicker than the usual type, without spiral turns and extraordinarily motile. Rise in temperature at the onset of an attack was associated with a rapid rise in the number of white blood corpuscles. During the interval the number fell again to normal or even below it. With succeeding attacks these variations became less marked. The thrombocytes were affected in the reverse manner. There was a fall in number during the attacks. The rate of sedimentation of the red blood corpuscles is generally increased during the incubation period and infection, though remissions may occur during the intervals between attacks.

C. M. W.

LEBEDJEVA (M.) & SSINJUSCHINA (M.). Die Salvarsanbehandlung des Rückfallfiebers bei Ratten. [**Salvarsan Treatment of Relapsing Fever in Rats.**]—*Arch. f. Dermat. u. Syph.* 1927. July 4. Vol. 153. No. 2. pp. 487–491. [6 refs.] [Educ. Commissariat R.S.F.S.R. & Bact. Inst., " 2. Universität," Moscow.]

Experiments have shown that it is not possible to eradicate a relapsing fever infection in all of a series of mice by means of salvarsan. In a varying percentage of animals the spirochaetes survive in the brain. Using rats for his experiments the author has found that they behave as mice have been found to do. He has also noted that as regards the number of animals which fail to be cleared of spirochaetes different strains of these organisms vary in their resistance to treatment.

C. M. W.

NICOLLE (Charles), ANDERSON (Charles) & COLAS-BELCOUR (Jacques). Sur un nouveau spirochète sanguicole pathogène (*Sp. normandi*) transmis par un Ornithodore (*Orn. normandi*), hôte des terriers de rongeurs nord africains. [**New Blood Spirochaete transmitted by *Ornithodorus* sp. living in Rodent Burrows.**]—*C.R. Acad. Sci.* 1927. Aug. 1. Vol. 185. No. 5. pp. 334–336.

——, —— & ——. Note préliminaire sur un nouveau spirochète sanguicole pathogène (*Sp. Normandi*) transmis par un Ornithodore (*Orn. Normandi*) hôte des terriers de rongeurs nord-africains.—*Arch. Inst. Pasteur de Tunis.* 1927. Sept. Vol. 16. No. 3. pp. 219–221. [1 ref.]

The tick *Ornithodorus normandi* inhabits the burrows of rodents, particularly those of the gerbil *Meriones shawi* in Tunis. Six of these ticks revealed, in the fluid obtained by crushing them, a spirochaete of the relapsing fever type which was inoculable to the mouse, rat and monkey. The name *Spirochaeta normandi* is given to this organism

Furthermore, a batch of nymphs and adults of the tick infected a gerbil by their bites while a captured gerbil was found to have a natural infection. Ticks collected near the spot where this gerbil was caught infected another gerbil by their bites. It was thus demonstrated that *Ornithodorus normandi* is the transmitting agent of a naturally occurring spirochaetosis of the gerbil. Attempts to transmit the spirochaete from monkey to monkey through the agency of lice failed. The new spirochaete differs from that of universal relapsing fever by the definiteness and duration of the infection in mice and by its transmission by the tick and not by the louse ; from that of Spanish relapsing fever by its non-transmission by the louse and absence of pathogenicity for the guineapig. It resembles those of African tick fever and the natural field vole infection (*Sp. crocidurae*). Serological investigations so far conducted substantiate the specificity of *Sp. normandi*. It seems possible that this organism might be transmitted to man, as it is known that *Ornithodorus normandi* will bite human beings.

C. M. W.

NICOLLE (Charles) & ANDERSON (Charles). Transmission du spirochète de la musaraigne par *Ornithodorus moubata* et mécanisme de la transmission des spirochètes récurrents par les tiques. [**Transmission of Field Vole Spirochaete by** *O. moubata*. **Mechanism of Transmission of Spirochaetes by Ticks.**]—*C.R. Acad. Sci.* 1927. Aug. 8. Vol. 185. No. 6. pp. 373–375.

—— & ——. Note préliminaire sur la transmission du spirochète de la musaraigne par *Ornithodorus moubata* et sur le mécanisme de la transmission des spirochètes récurrents par les tiques.—*Arch. Inst. Pasteur de Tunis.* 1927. Sept. Vol. 16. No. 3. pp. 222–224. [1 ref.]

The naturally occurring field vole spirochaete of Dakar (*Sp. crocidurae*) is shown to be transmissible by *Ornithodorus moubata*, the vector of the spirochaete of African tick fever (*Sp. duttoni*). Nymphs fed on infected animals will transmit the infection when fed again on healthy ones. Adults fed on infected animals are unable to transmit the infection, but the nymphs of the next generation, hereditarily infected, are able to do so. Whether adults developing from infective nymphs are infective is not yet known, though this seems possible, since the authors have demonstrated it in the case of the spirochaete of Spanish relapsing fever and *Ornithodorus marocanus*. They have also shown that adults of *O. marocanus* fed on infected animals are unable to infect other animals. It is known, however, from the experiments of ORTEGA that the infection can be passed to the nymphs of the next generation. These experimental results are in support of the authors' opinion that in the tick-transmitted infections the principal vectors are the nymphs and that the small mammals are the hosts of preference for the spirochaetes ; the transmission by adult ticks and the infection of large mammals, particularly man, are of recent introduction and play no part in the natural maintenance of the virus.

A word of warning is given to those who assume that because the fluids from crushed ticks are infective the ticks are therefore transmitters of the particular virus : only the natural method of infection should be taken into account in drawing such conclusions.

C. M. W.

BRUMPT (E.). Transmission du *Treponema crocidurae* par deux *Ornithodorus* (*O. moubata* et *O. marocanus*). [**Transmission of *T. crocidurae* by Two Species of Ornithodorus.**]—*C.R. Acad. Sci.* 1926. Dec. 6. Vol. 183. No. 23. pp. 1139–1141.

The spirochaete *Treponema crocidurae* which was discovered by ANDRÉ LEGER in 1917 in the field vole, *Crocidura stampfli*, of Dakar has since been found to occur naturally in various rats and mice in the same locality, viz., *Mus decumanus, Mus coucha, Golunda campanae.* The spirochaete, which is morphologically identical with the relapsing fever spirochaetes, is inoculable to human beings, monkeys and the ordinary laboratory animals. The author has now shown that nymphs of both *Ornithodorus moubata* and *O. marocanus* can retain the virus after feeding on infected mice for 30 and 25 days respectively. The nymphs were fed on the mice, kept till they had moulted and then crushed and injected into other mice. It is concluded that the spirochaete is transmissible by both these ticks. In a footnote it is stated that *Treponema hispanicum*, the relapsing fever spirochaete of Spain, which is transmitted in nature by *Ornithodorus marocanus*, may also be transmitted by *O. moubata* and *Haemaphysalis inermis.* Details of the experiments are not given, but presumably they are of the kind noted above. [In papers by NICOLLE and ANDERSON reviewed above it is stated that this type of experiment does not prove that the ticks are actual transmitters.]

C. M. W.

NICOLLE (Charles) & ANDERSON (Charles). Transmission expérimentale du spirochète de la récurrente espagnole par l'*Ornithodorus moubata* et mécanisme de cette transmission. [**Transmission of Spirochaete of Spanish Relapsing Fever by *O. moubata*. Its Mechanism.**]—*C.R. Acad. Sci.* 1927. Aug. 22. Vol. 185. No. 8. pp. 433–434.

—— & ——. Note préliminaire sur la transmission expérimentale du spirochète de la récurrente espagnole par l'*Ornithodorus moubata* et mécanisme de cette transmission.—*Arch. Inst. Pasteur de Tunis.* 1927. Sept. Vol. 16. No. 3. pp. 225–227. [1 ref.]

Experiments conducted with the spirochaete of Spanish relapsing fever have shown that it may be transmitted by *Ornithodorus moubata*, which is not its natural vector. The adults, which can harbour spirochaetes for long periods, are not themselves capable of transmitting them by their bites. The nymphs bred from such adults are able to do so, but only at their second feed on an animal. Thus *O. moubata* in addition to being the natural vector of the spirochaete of African tick fever is able also to transmit by the bite of the nymph the naturally occurring field vole spirochaete (*Sp. crocidurae*) and that of Spanish relapsing fever.

C. M. W.

NICOLLE (Charles) & ANDERSON (Charles). Sur la résistance du porc au virus de la fièvre récurrente espagnole et sur les conditions naturelles d'existence de cette maladie et d'autres spirochétoses. [**Resistance of the Pig to Spanish Relapsing Fever.**]—*C.R. Acad. Sci.* 1927. May 30. Vol. 184. No. 22. pp. 1305–1306.

In his original account of the transmission of relapsing fever in Spain by *Ornithodorus marocanus* (this *Bulletin*, Vol. 23, p. 590) DE

BUEN pointed out that the tick never lived away from pigs, and it was naturally suggested that the pig would be found to be the reservoir of the virus. The authors of the paper under review have attempted to infect pigs by inoculating them with virulent blood, but without effect. As a result they suggest that the reservoir of the virus is likely to be found amongst the small rodents which live in and around the pig stys and which would serve as more suitable hosts for the young ticks than the thick-skinned pigs. [In the review of DE BUEN'S paper in this *Bulletin* (*loc. cit.*) the reviewer erroneously stated that pigs had been infected by the injection of crushed ticks. Actually the injection failed to produce an infection.]

C. M. W.

GWÉLESSIANY (J.). Recherches sur le passage des spirochètes à travers les muqueuses et la marche des infections mixtes spirochéto-trypanosomiennes. [**Penetration of Mucosa by Spirochaetes Alone and in Mixed Infections with Trypanosomes.**]—*Bull. Soc. Path. Exot.* 1927. July 13. Vol. 20. No. 7. pp. 653–664. [27 refs.] [Pasteur Inst., Paris.]

The experiments of IWANOFF and MESNIL which demonstrated that, contrary to the generally accepted view, *Trypanosoma equiperdum* was unable to pass through a healthy mucous membrane [see this *Bulletin*, Vol. 24, p. 972] led the author to reinvestigate the relapsing fever spirochaetes from the same point of view. As in IWANOFF and MESNIL'S experiments the greatest care was taken to exclude the possibility of an injured mucosa by keeping the animals to be used under conditions of food and fodder that could not produce the slightest abrasion. Before applying infective material the mucous membrane was carefully examined with a lens. As a control *Trypanosoma equiperdum* was used. The outcome was that it was demonstrated that both *Treponema duttoni* and *T. crocidurae* were able to pass through the healthy mucosa of the mouth or eye. When a mixture of spirochaetes and trypanosomes was applied the spirochaetes alone penetrated.

C. M. W.

STEINER (G.) & STEINFELD (J.). Experimentelle Untersuchungen zur Pathologie und Therapie der Spirochätenkrankheiten. Parabiose bei experimenteller Recurrens. [**Pathology and Therapy of Spirochaete Diseases. Parabiosis.**]—*Klin. Woch.* 1927. Aug. 20. Vol. 6. No. 34. pp. 1597–1599. [11 refs.] [Psychiat. Clinic Univ. Heidelberg.]

Various investigations have shown that when mice have recovered from experimental relapsing fever spirochaetes persist in the brain substance for long periods as demonstrated by inoculating brain emulsion into healthy mice. In no circumstances do these latent spirochaetes ever reinvade the blood stream which with its antibodies appears to act as an impenetrable barrier. The authors have treated the mice in many ways in order to bring about such an invasion but without result. They now describe a further attempt which consisted in uniting parabiologically a healthy and a recovered animal with a view to discovering whether the healthy animal would be invaded with spirochaetes. No such invasion occurred, the healthy united animal

quickly acquiring a passive immunity. It was demonstrated that if one of two healthy united animals were inoculated with spirochaetes both acquired an infection. [AZNAR, in a paper reviewed in this number, records the return of spirochaetes to the blood under the influence of a trypanosome injection.]

C. M. W.

BRUYNOGHE (R.) & DUBOIS (A.). L'utilisation des glucides par *Spirochaeta duttoni*. [**Use of the Glucides by** *S. duttoni*.]—*C. R. Soc. Biol.* 1927. May 27. Vol 96. No. 17. pp. 1403–1404. [1 ref.]

Having shown that trypanosomes which have become immobile may be revitalized by the addition to the medium of various sugars, particularly glucose, the author wished to discover whether spirochaetes were similarly affected. Very fair infections of spirochaetes (*T. duttoni*) could be obtained in mice if they were inoculated with both spirochaetes and trypanosomes. At the moment when the trypanosomes were very numerous and had produced a hypoglycaemia it was noted that the spirochaetes were even more susceptible than the trypanosomes, for they became motionless sooner. If sugar solution be added to a suspension in which both organisms have become immobile the mobility returns. When artificial hypoglycaemia was produced by means of insulin, though the results were not very definite, it was clear that the spirochaetes taken before the administration of insulin remained mobile for a longer time than those taken after it. It is concluded that the glucides are indispensable for the metabolism of spirochaetes, particularly for their powers of movement.

C. M. W.

LEBEDJEWA (M.). Die elektive Lokalisation der Recurrensspirochäten im Nervengewebe. [**Affinity of Relapsing Fever Spirochaetes for Nerve Tissues.**]—*Arch. f. Dermat. u. Syph.* 1927. July 4. Vol. 153. No. 2. pp. 531–535. [13 refs.] [Educ. Commissariat, Moscow.]

An investigation of the brain, liver, spleen and kidneys of mice infected with relapsing fever spirochaetes has shown that the organisms are only occasional parasites of the blood. They show a marked affinity for the tissues of the nervous system.

C. M. W.

KRITSCHEWSKI (I. L.). Die experimentellen Grundlagen der Lehre von den neurotropen und somatropen Rassen der Spirochäten. [**Neurotropic and Somatotropic Races of Spirochaetes. Experimental.**]—*Klin. Woch.* 1927. July 16. Vol. 6. No. 29. pp. 1370–1374. [13 refs.] [Educ. Commissariat, R.S.F.S.R., Moscow.]

Inoculating mice with three races of relapsing fever spirochaetes it was found that they differed as regards their persistence in the central

nervous system of the animals. One race persisted in 16·1 per cent. of the animals, the figures for the two other races being 39·6 and 78·6. The last is thus definitely more neurotropic than the others. It is possible that there is a similar difference between races of *Treponema pallidum.* The author claims that he has produced the first experimental evidence of the existence of neurotropic as distinct from somatropic races of spirochaetes.

C. M. W.

BROWNING (C. H.), COHEN (J. B.), GULBRANSEN (R.), PHILLIS (E.) & SNODGRASS (W. R.). **The Therapeutic Action of Some Bismuthyl Derivatives of Organic Hydroxy-Acids.**—*Proc. Roy. Soc.* 1927. Aug. 2. Ser. B. Vol. 102. No. B713. pp. 1–9. [10 refs.] [St. George's House Med. School, Leeds. Path. Dept. Univ. & Western Infirmary, Glasgow.]

This is a study of the therapeutic action, in mice infected with *Spirochaeta laverani*, Breinl and Kinghorn, and *Sp. muris*, Wenyon, of a series of analogues of bismuthyl tartaric acid, in which tartaric acid is replaced by other organic hydroxy-acids. The preparation and composition of these substances are recorded and suggestions made as to their constitution. All of them produced definite therapeutic action as shown by disappearance of parasites from the blood, but in most cases the organisms re-appeared even after doses approaching the maxima tolerated. There is distinct evidence throughout the series that the therapeutic efficacy is not directly proportional to the amount of bismuth present, and since only the saccharic, mannonic, lactobionic and citric acid derivatives are curative the organic acid component of the molecule must exert some influence. Bismuthyl saccharic acid was tried in human syphilis, but showed no advantage over bismuth compounds already in use. Bismuthyl gluconic acid is still under trial in human syphilis.

T. A. Henry.

BJERLÖW (H.) & LILJESTRAND (G.). **The Resting Minute Volume of the Heart in Man during Recurrent Fever.**—*Acta Med. Scandinavica.* 1927. Vol. 67. No. 1–2. pp. 5–13. [8 refs.] [" Karolinska " Inst., Stockholm.]

As a result of experiments on four patients, in whom fever was produced by the inoculation of relapsing fever spirochaetes, it was noted that standard metabolism showed a typical rise with rise of temperature while the utilization of the oxygen of the blood remained constant. There was thus a rise, during fever, in the minute volume of the heart which was in direct proportion to the rise in oxygen consumption.

C. M. W.

LUENGO (E.). La fièvre récurrente en Espagne. [**Relapsing Fever in Spain.**]—*Bull. Office Internat. d' Hyg. Publique.* 1927. July. Vol. 19. No. 7. pp. 931–933. [1 ref.]

A short account of relapsing fever in Spain and the observations of DE BUEN incriminating *Ornithodorus marocanus* as the vector.

C. M. W.

SANARELLI (G.). Identité entre spirochètes et bacilles fusiformes. Les héliconèmes "Vincenti." [**Identity of Spirochaetes and Fusiform Bacilli.** *Heliconema vincenti.*]—*Ann. Inst. Pasteur.* 1927. July. Vol. 41. No. 7. pp. 679–720. With 1 text fig. & 24 figs. on 2 plates. [65 refs.]

——. Identità degli Spirocheti e dei Bacilli fusiformi. Gli "*Heliconema vincenti.*"—*Ann. d'Igiene.* 1927. Sept. Vol. 37. No. 9. pp. 569–603. With 1 text fig. and 24 figs. on 2 plates. [65 refs.]

In a previous number of this *Bulletin* (Vol. 24, p. 698) a long paper by the author on the cultivation of the caecal spirochaetes of guineapigs was reviewed. Further observations are now recorded which are of considerable interest since they throw light on the vexed question of the significance of the numerous saprophytic spirochaetes which have been described as the cause of so many varied pathological conditions. The author has noted that abundant growth of this organism can be obtained in Tarozzi's medium which consists of agar slopes with a piece of fresh guineapig tissue in each. If very large doses are injected into the peritoneal cavity of guineapigs death is produced in a few hours. Large numbers of small spirochaetes are found in the cavity while the organisms may be recovered by culture from the heart blood or organs. If the peritoneal exudate is collected and sub-inoculated to other guineapigs no effect is produced. In old cultures the coccus forms occur in large numbers but a few spirochaetes may be found so that it is impossible to state finally that the spirochaetes which appear in sub-culture have developed exclusively from the coccus forms. The difficulty of cultivating the spirochaete in ordinary broth was noted in the previous paper. It has now been found that if the broth is inoculated with *Bacillus mesentericus vulgatus* and at the same time with the spirochaete extraordinarily rich cultures are obtained. Furthermore the same result is obtained if the spirochaetes are inoculated into the bacteria-free filtrate of a culture of this bacillus. The substance in the filtrate which favours the growth of the spirochaete is probably of the nature of an enzyme, for it is thermolabile. The substance has another action on the spirochaetes, for it leads to the production from them of fusiform bacilli, thus demonstrating that these organisms are actually developed from spirochaetes. As a rule this fusiform stage will revert to the spirochaete form in sub-culture, but conditions are described which lead to the stabilization of the fusiform stage which persists in sub-culture. These fusiform bacilli inoculated to animals in sufficient doses will kill them. Sub-culture from the organs or blood will give mixed cultures of fusiform bacilli and spirochaetes. Guineapigs immunized against the spirochaetes will develop agglutinins which act in equal titres against both the spirochaetes and fusiform bacilli and vice versa. By dark ground observation the origin of the fusiform bacilli has been studied. It appears that under certain conditions the spirochaetes lose their power of revolving on their longitudinal axes, and they become filaments or actually bands. These bands twisted at intervals produce in stained films the appearance of a number of fusiform elements attached end to end. When division occurs at the twisted points a number of separate fusiform elements, the fusiform bacilli, are produced. It is suggested that this polymorphic organism, which embraces in its morphology many types of spirochaete and fusiform bacilli described from man, should be named *Heliconema vincenti.*

C. M. W.

KANAGARAYER (K.). **Spirochaetal Pulmonary Gangrene.**—*Malayan Med. Jl.* 1927. Vol. 2. No. 2. pp. 58–60. [3 refs.] [Inst. Med. Research, Kuala Lumpur.]

Seven cases of pulmonary gangrene are described in which spirochaetes and fusiform bacilli were found either in the sputum or gangrenous areas in the lungs. The organisms were indistinguishable from those in Vincent's angina, dental caries, pyorrhoea alveolaris and bronchial spirochaetosis. All the cases developed during the course of pneumonia as a result of invasion from oral, dental, tonsillar or bronchial lesions. In Malaya pneumonia is if anything more common amongst Tamils than Chinese but pulmonary gangrene is more common amongst Chinese, who also show a greater incidence of oral lesions.

C. M. W.

SMITH (Curtis E.) & RUSK (G. Y.). **Pulmonary Spirochetosis.**—*Amer. Jl. Path.* 1927. May. Vol. 3. No. 3. pp. 225–233. With 4 figs. on 2 plates. [9 refs.]

As a result of the study of the lungs in certain fatal cases in which spirochaetes were found in the sputum before death the authors suggest that the serious pathological conditions would still have been present if the lungs had never become infected with spirochaetes, which are frequently found in the sputum and lung tissues of patients with pulmonary abscess or gangrene. The frequent association of fusiform bacilli suggests that the spirochaetes may be of the Vincent type and not a definite entity. All forms of pulmonary spirochaetosis probably represent secondary infection. The presence of spirochaetes in large numbers, deeply situated in the tissue, suggests some pathogenic influence.

C. M. W.

ARAVANTINOS (Jean D.). Un cas de bronchite sanglante de Castellani. [**Bloody Bronchitis of Castellani.**]—*Grèce Méd.* 1927. Mar.–Apr. Vol. 29. No. 3–4. pp. 14–16. [4 refs.]

A case of bronchial spirochaetosis with haemoptysis which recovered under a course of stovarsol treatment.

C. M. W.

VINCENT (H.). Sur la fuso-spirochétose des voies respiratoires. Sa localisation bronchique. [**Fuso-Spirochaetosis of the Respiratory Tract.**]—*Bull. Acad. Méd.* 1926. Oct. 19. Year 90. 3rd Ser. Vol. 96. No. 33. pp. 135–145. [2 refs.]

This is a long argument in defence of the position that the organism of bronchial spirochaetosis is no other than that of Vincent's angina.

C. M. W.

RAT-BITE FEVER.

RUYS (A. Charlotte). Zweedraadkleuring voor den spiril van de rattebeetziekte. [**Classification of the Organism of Rat-Bite Fever.**] —*Geneesk. Tijdschr. v. Nederl.-Indië.* 1926. Vol. 66. No. 6. p. 800. With 1 plate.

——. Klassifikation des Erregers der Rattenbisskrankheit.—*Cent. f. Bakt.* 1. Abt. Orig. 1927. Aug. 5. Vol. 103. No. 4-5. pp. 268–270. With 8 text figs. [4 refs.] [Inst. Trop. Hyg., Amsterdam.]

These notes emphasize the difference between the organism of rat bite fever and true spirochaetes. The movements are not those of a spirochaete, while suitable staining demonstrates numerous flagella at each end and not a single one as figured by NOGUCHI (1926). That the organism was more nearly related to the spirilla was first shown by ADACHI (*Jl. Exper. Med.*, 1921, Vol. 33, p. 647) and later by ZUELZER (*Cent. f. Bakt.* I. Abt. Orig., 1921, Vol. 85, p. 154*). The author agrees with these conclusions, which have been drawn also by ROBERTSON (this *Bulletin*, Vol. 22, p. 179). The papers are illustrated by a series of good microphotographs.

C. M. Wenyon.

HEITZMANN (Otto). Vergleichende pathologische Anatomie der experimentellen Rattenbisskrankheit und der Infektion mit Mäusespirillen. [**Comparative Pathology of Experimental Rat-Bite Fever and Infection with Mouse Spirilla.**]—*Arch. f. Dermat. u. Syph.* 1927. July 4. Vol. 153. No. 2. pp. 399–406. [10 refs.] [Reich Health Office, Berlin-Dahlem.]

An examination of the tissues of guineapigs infected with the organism of rat bite fever and the naturally occurring and similar organism of mice has shown that the histopathological changes produced are the same. This affords additional evidence of the identity of the two organisms.

C. M. W.

CILENTO (R. W.). **Rat Bite Fever in New Guinea.** —*Med. Jl. Australia.* 1927. Aug. 6. Vol. 2. No. 6. pp. 191–193. With 1 chart. [1 ref.]

A patient who came under observation on December 9th in New Guinea after having had attacks of fever since October. His blood showed rings of subtertian malaria and he was treated with quinine. The temperature, however, did not respond, and he was admitted to Rabaul Hospital on December 30th. There were no malarial parasites in the blood, and on account of the relapsing type of fever of six-day periodicity the case was diagnosed provisionally as one of relapsing fever. Later the patient stated that he had been bitten on the thumb on November 6th by a flying squirrel, and that twelve days later the wound had festered and had led to lymphangitis. This suggested "rat bite fever." Blood examination was instituted, and with the dark ground "a short organism was distinctly seen which appeared to resemble a leptospira rather than a spironeme, and was apparently about 6μ in length." Subsequent drops of blood revealed occasional organisms of the same type. A diagnosis of rat-bite fever was made and treatment with novarsenobenzol instituted. The patient was discharged cured on February 5th.

[The accuracy of the diagnosis is unfortunately invalidated by the account of the organism. It is hardly possible for the spirillum of rat-bite fever to be mistaken for a leptospira.]

C. M. W.

RUBINO (Anthony P.). **Two Cases of Rat-Bite Fever.**—*Public Health Rep.* 1927. Aug. 19. Vol. 42. No. 33. pp. 2097–2099.

Two cases of rat-bite fever in a man 42 years of age and his son 17 years of age, both of whom were bitten while catching rats for experimental purposes. The diagnosis was based on the intermittent relapsing fever following rat bite, the regional lymphadenitis without suppuration, the characteristic exanthem and the response to neosalvarsan treatment.

C. M. W.

SALIMBENI (A. T.) & SAZERAC (R.). Action du bismuth sur le spirochète du Sodoku dans l'infection expérimentale du cobaye. [**Action of Bismuth on the Sodoku Spirochaete in Guineapig Experiment.**]—*C.R. Acad. Sci.* 1927. June 13. Vol. 184. No. 24. pp. 1497–1499.

By emulsifying in 10 cc. of physiological saline solution the spleen of a mouse infected with the organism of rat bite fever and filtering through metallic gauze a fluid is obtained which will produce in guineapigs an acute (15–20 days) or a chronic (2–3 months) infection according to the dose of virus employed. The chronic infection is best produced by injecting 1 cc. of the filtered emulsion. Ten guineapigs were each given a subcutaneous injection of tartrobismuthate of soda (1 in 100 aqueous solution) in a dose of 1 centigram for each 100 grams of body weight. One hour later these 10 animals and 10 controls were given subcutaneously 0·5 cc of virus. After 2 or 3 days incubation there developed at the site of inoculation in all the controls an area of infiltration which increased in size and developed into a veritable chancre in which the causative organism was demonstrated. The organism appeared in the blood between the 8th and the 11th day. The other mice developed no infection, thus demonstrating that the drug had completely protected them. Using the drug as a curative agent after infection had been established it was possible to produce only a remission of symptoms which reappeared in 10 to 12 days A further dose brought about another similar remission, but a definite cure was not obtained. It is thus evident that bismuth has a definite action on the organism of rat bite fever.

C. M. W.

NAKAMURA (Sohji). [**On the Complement Fixation Reaction in Rat-Bite Fever.**]—*Kei-O Igaku (Jl. Kei-O Med. Soc.).* 1926. July. Vol. 6. No. 7. [Summarized in *Japan Med. World.* 1927. Mar. 15. Vol. 7. No. 3. pp. 79–80.]

A rat-bite fever reactive substance and a haemolysin appear in the serum of experimentally infected rabbits. The former is destroyed by administration of salvarsan to a rabbit which is developing these substances. For the haemolytic reaction it was necessary to add both visceral extracts and cholesterine.

C. M. W.

INFECTIOUS JAUNDICE AND OTHER LEPTOSPIROSES.

LANGWORTHY (Virginia) & MOORE (Anna C.). **A Study of** *Leptospira icterohaemorrhagiae.*—*Jl. Infect. Dis.* 1927. July. Vol. 41. No. 1. pp. 70–91. With 2 figs. [83 refs.] [New York State Dept. of Health, Albany.]

Reference is again made to the outbreaks of infectious jaundice which occurred in New York State during autumn 1921 and the winter of 1922 (see this *Bulletin*, Vol. 19, p. 561). Further work has been done, particularly in connexion with the leptospira found in rats. It seems clear that the outbreaks of jaundice referred to were not of leptospiral origin and that the etiology is still unknown. As regards rats leptospira was demonstrated in over 40 per cent. of the animals while immunological tests with rat sera showed that over 60 per cent. were infected. The organism isolated from these Albany rats after exhaustive investigations was found to be apparently identical with *Leptospira icterohaemorrhagiae.* The instance of the human being who was accidentally infected in the laboratory with one of the rat strains is again mentioned. Even 4 years after recovery the serum of this person gave marked protection to guineapigs against virulent strains of *L. icteroides* and *L. icterohaemorrhagiae.*

C. M. Wenyon.

TOWLER (Harry H.) & WALKER (John E.). **Spirochetal Jaundice. Report of a Case.**—*Jl. Amer. Med. Assoc.* 1927. July 9. Vol. 89. No. 2. pp. 86–89. [31 refs.] [Walter Reed General Hosp. & Army Med. School.]

The paper describes a typical case of leptospiral jaundice, this being the sixth proved case to be reported in North America. Guineapigs were infected by inoculation with the patient's blood on the ninth day of the illness. They showed the characteristic lesions while cultures of the organism were obtained from their blood.

C. M. W.

MACKIE (T. J.) & MCLACHLAN (D. G. S.). **Report of an Investigation into an Outbreak of Infectious Jaundice.**—*Edinburgh Med. Jl.* 1927. Aug. N.S. Vol. 34. No. 8. pp. 456–465. [12 refs.] [Bact. Dept., Edinburgh Univ.]

The paper describes an outbreak of infectious jaundice comprising four cases at a farm near Cumnock, Ayrshire, and three at a " cothouse " about a mile and a half distant. The illness was of an exceedingly mild type, of short duration and followed by rapid convalescence. Young persons only were affected and there was a familial incidence. A laboratory investigation of urine from four cases revealed " atypical leptospiras " in three. In two cases the organisms were inoculated into guineapigs. From one case two were inoculated—one of these animals died on the 20th day and showed " spotted " haemorrhages in the lungs and also haemorrhages in the diaphragm, kidneys, stomach wall and axillae. There was no jaundice and no leptospiras could be found. The other animal which had been ill was killed on the 15th day and showed irregular haemorrhages in the lungs. From another

case one guineapig was inoculated with the urine deposit. It died on the 8th day and showed haemorrhages in the lungs and kidney, and as in the other animals no leptospiras were seen and sub-inoculations were negative. As regards the intervals between the cases in the two families, the last case in each occurred at an interval of about a month after the onset of the previous case. Though the absolute proof has not been obtained it would seem possible that the outbreak was due to a strain of *Leptospira icterohaemorrhagiae* of low virulence.

C. M. W.

MELNOTTE (Pierre) & FARJOT (Antonin). La spirochétose ictérigène au Maroc. [**Spirochaetal Jaundice in Morocco.**]—*Arch. Inst. Pasteur d'Algérie.* 1927. Mar. Vol. 5. No. 1. pp. 41–47. [" Auvert " Hosp., Fez.]

During 1925 and 1926 the authors have seen seven cases which corresponded clinically with those of infectious jaundice. Spirochaetes were discovered in the urine of six, but guineapigs inoculated from two of the cases did not become infected. In two cases there was a complication—malaria in one and paratyphoid A in the other. All the cases terminated in recovery. It is admitted that the diagnosis is incomplete in that guineapigs were not infected and serological tests were not made. In view of these cases it is suggested that facilities for carrying out these tests should be instituted in Morocco. It is noted that spirochaetes were seen in a kidney smear of a rat captured near the habitations of the patients.

C. M. W.

MORISSEAU (R.). Considérations cliniques sur quelques spirochétoses ictéro-hémorragiques à forme épidémique. [**Epidemic Icterohaemorrhagic Spirochaetoses.**]—*Rev. Méd. et Hyg. Trop.* 1927. May–June. Vol. 19. No. 3. pp. 84–86.

For several years a spirochaetosis has been recognized in French West Africa which, rapidly acquiring an epidemic character, attacks first the natives and then the Europeans. The symptoms are often serious and comprise violent headache, bilious vomiting, lumbar pains and a temperature of 39 to 40° C. After a remission there is a further rise in temperature, the vomit becoming black and haemorrhagic, with haemorrhages and epistaxis. Sometimes there is recovery but more usually a fatal issue. An epidemic of the kind was seen by Dr. STEVENEL at Bouaké on the Ivory Coast. Spirochaetes with some resemblance to Noguchi's leptospira were seen in the blood but stegomyia was so rare that a diagnosis of yellow fever could not be made. Another centre of infection was noted at Mankouo by Dr. BLANQUIER. In this case it appeared possible that there was a water origin of the epidemic, as the natives were compelled to take their water from a highly contaminated source. A third epidemic was seen at Toukoto by Dr. BRAY. In this case the Europeans alone were involved, the natives, in the midst of whom the Europeans lived, being regarded as reservoirs of the virus.

C. M. W.

Jo (Masanori). Ueber die Pathogenese des Ikterus bei der Spirochaetosis icterohaemorrhagica (Weil'sche Krankheit). [**Pathogeny of Jaundice in Weil's Disease.**]—*Scientific Reports Govt. Inst. Infect. Dis.* Tokyo. 1926. Vol. 5. pp. 283–285. With 7 figs. on 2 plates (1 coloured). [5 refs.]

An investigation of the histopathology of Weil's disease together with the bilirubin reaction of the blood serum and the changes in the bile has led the author to the conclusion that the jaundice is not, in the early stages at least, an obstructional jaundice. It is due rather to an over production of bile pigments as a result of increased red cell destruction combined with a loss of function by the damaged liver cells.

C. M. W.

Bernard (Etienne) & Gilbert-Dreyfus. Rôle de l'action hypothermisante de l'azotémie sur la courbe thermique de la spirochétose ictérigène. Recrudescence fébrile et rechute hypothermique. [**Azotaemia and Fall of Temperature in Leptospiral Jaundice.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1927. Nov. 10. Year 43. 3rd Ser. Vol. 51. No. 31. pp. 1467–1485. With 5 text figs. [22 refs.]

The paper is a lengthy discussion of the cause of the fall in temperature followed by a relapse which was observed in a case of leptospiral jaundice. It was noted that the patient was in the most serious condition after the temperature had fallen and before the relapse. As in other infections a similar fall in temperature had been found to be associated with an increase in the nitrogenous substances of the urea group of the blood. In fact the quantity of these substances present varied inversely with the temperature. It is concluded that the fall in temperature between the initial attack and relapse in leptospiral and other spirochaete infections is not due to a remission of the disease, but to the temperature being forced down by the increasing intensity of the azotaemia.

C. M. W.

i. Sazerac (R.) & Nakamura (Hirosi). Pouvoir préventif et pouvoir curatif du bismuth vis-à-vis du "Spirochaeta icterohaemorragiae." [**Bismuth in the Prevention and Cure of Icterohaemorrhagic Spirochaetosis.**]—*Bull. Acad. Méd.* 1927. June 7. Year 91. 3rd Ser. Vol. 97. No. 23. pp. 774–776. [4 refs.]

ii. Sazerac (R.), Hosoya (S.) & Stefanopoulo (G.). Action du bismuth sur le "*Leptospira icteroïdes*" (agent infectieux de la fièvre jaune, d'après Noguchi).—*Bull. Acad. Méd.* 1927. July 26. Year 91. 3rd Ser. Vol. 98. No. 30. pp. 152–153. [4 refs.]

i. Experiments similar to those detailed above (p. 98), have been conducted with *Leptospira icterohaemorrhagiae.* Tartrobismuthate of soda will not only protect guineapigs against infection but will bring about a cure if given before the fourth day of an infection. By re-inoculating animals at varying intervals after recovery following treatment it was found that the protective action of the drug might persist as long as five months.

ii. Similar experiments have been conducted with a strain of *Leptospira icteroides* which produced death in guineapigs in 4 days. Very similar results were obtained, a fact which affords additional evidence of the close relationship of *L. icteroides* and *L. icterohaemorrhagiae*.

C. M. W.

WALCH (E. W.) & WALCH-SORGDRAGER (G. B.). **Observations on *Leptospira icterohaemorrhagiae* in the Wild Rats of Baltimore.**—*Amer. Jl. Hyg.* 1927. July. Vol. 7. No. 4. pp. 393–406. With 1 plate. [22 refs.] [Sch. of Hyg. & Pub. Health, Johns Hopkins Univ.]

The examination of 51 Baltimore rats (*Mus norvegicus* and *Mus decumanus*) during the period November, 1924, to January, 1925, resulted in the discovery of leptospira in 17 (33 per cent.). Of the 17 strains 6 were virulent to guineapigs and of these 2 could be transmitted from animal to animal. Serologically there was evidence that the Baltimore strain was the same as those of other cities. Of 9 filtration experiments with virulent liver emulsions diluted fifteen times, through Berkefeld candles V, one filtrate was obtained which caused death with typical symptoms when injected into two guineapigs, though no leptospira could be seen in it. Filtering young virulent cultures through Berkefeld candles V, N and W yielded filtrates in which leptospira could always be detected.

C. M. W.

i. WILBERT (R.). Sur une maladie infectieuse du chimpanzé, transmissible à l'homme. [**An Infectious Disease of the Chimpanzee Transmissible to Man.**]—*C.R. Acad. Sci.* 1927. Sept. 12. Vol. 185. No. 11. pp. 569–571.

ii. —— & DELORME (M.). Sur une spirochétose ictéro-hémorrhagique du chimpanzé transmissible à l'homme.—*Ann. Inst. Pasteur.* 1927. Nov. Vol. 41. No. 11. pp. 1139–1155. [8 refs.] [Pasteur Inst., Kindia, French Guinea.]

i. In January of this year the Institut Pasteur of Kindia received six chimpanzees from the Ivory Coast. Nine other animals died en route. The six which arrived did not appear happy, and had capricious appetites. On 13th March an epizootic broke out amongst the chimpanzees, which included 17 others which had come from Guinea. All died, except one which recovered, in 16 to 11 days. The main symptoms were fever, which reached 40·8° to 41° C. falling to 36° C. before death, general prostration and embarrassed respiration, congestion and sub-icteric tinging of the conjunctivae, swelling of the abdomen with hyperaesthesia especially of the epigastric region, haemorrhagic vomit and constipation followed by diarrhoea. At autopsy there was found sub-icterus, suffusions of blood, pulmonary infarcts, peritonitis, congestion and localized gangrene of the intestine, slight enlargement of the spleen, fatty degeneration of the liver, petechial haemorrhages in the gastric mucosa, altered kidneys, injection with haemorrhagic spotting of the central nervous system, cerebro-spinal fluid turbid and bloodstained. There was further a polynuclear increase while the urine was greenish in colour and contained albumin. In the blood, liver, spleen, kidneys and nervous system was found a spirochaete which

performed slow rotary movements and measured 6·7 by 0·2 microns. It stained like other spirochaetes and was cultured in N.N.N. medium and in rabbit blood medium. The organisms survived in the cultures for 12 to 25 days. Nothing is said of sub-culture. It is stated that the virus is transmissible to the chimpanzee, to the guineapig and also to man, as occurred in the case of the author, who showed the following symptoms—rectal temperature 40·6° C., congested conjunctivae, subicterus, scanty urine, anorexia, vomiting, delirium and nightmare, asthenia and an attack of haemorrhagic cystitis. The spirochaete occurred in the blood which inoculated to a chimpanzee brought about its death. The investigation was not pursued any further.

The author thinks that yellow fever should be considered, but it must be admitted that the statements, especially those about the spirochaetes, are not entirely satisfactory. Was he dealing with pseudospirochaetes or blood filaments ?

ii. The second paper describes the same outbreak but in greater detail. It is noted that the rats which visited the cages of the chimpanzees at night were found to be carriers of spirochaetes which, however, were larger and more active than those found in the chimpanzees, the animals inoculated from them, the cultures from the first author who contracted the disease and in the cultures. The chimpanzee inoculated with 3 cc. of the author's blood, in which a few rare spirochaetes were found, died in 1½ days after showing the same symptoms. The name *Spirochaeta anthropopitheci* n. sp. is suggested for the organism, the more detailed account of which does not entirely remove all doubt as to its actual nature.

C. M. W.

Klarenbeek (A.). Présence de spirochètes du type *Leptospira* dans les reins des chiens atteints d'ictère et de fièvre typhoïde. [**Leptospira in the Kidneys of Dogs with Jaundice and Typhoid Fever.**]—*Ann. Inst. Pasteur.* 1927. Nov. Vol. 41. No. 11. pp. 1156–1165. With 5 text figs. [18 refs.] [Vet. Faculty, Utrecht, & Pasteur Inst., Paris.].

——. Een leptospirose als oorzaak van icterus van den hond.—*Tijdschr. v. Diergeneesk.* 1927. Nov. 15. Vol. 54. No. 22. pp. 1041–1045. [5 refs.] English summary pp. 1045–1046. [Veterinary Med. Faculty, Univ. Utrecht.]

The paper describes an acute and fatal disease which attacks young dogs in Utrecht. The symptoms are apathy, jaundice, haemorrhage in the skin and mucosae, vomiting and passage of blood with the faeces, a normal or subnormal temperature. After death, which occurs in about a week, there is found hypertrophy and softening of the liver, degeneration of the kidneys and haemorrhages in the lungs, viscera and mucosa of the digestive tract. Sections of the kidneys of a number of dogs revealed spirochaetes in three. In the fresh blood the spirochaetes in their structure and movements resembled the leptospira of Weil's disease. They were not discovered in the urine. It was not possible to infect guineapigs from either the blood or the urine. It is concluded that the disease resembles the leptospiral jaundice described in English dogs by Okell, Dalling and Pugh (*Vet. Jl.*, 1925, Vol. 81, p. 3), which, however, was transmissible to guineapigs.

In 1924 LUKES described as typhoid fever a disease of dogs in Stuttgart (*Trop. Vet. Bull.*, Vol. 13. p. 56) which he claimed was due to a spirochaete. The author has been able to examine a number of cases of this disease, the symptoms of which, like the Utrecht infections, appear to result from damage to the kidneys. In sections of these organs stained by Levaditi's silver nitrate method leptospira was demonstrated in abundance either within or on the surface of the renal epithelium. It would appear that the damage caused to the kidneys by the leptospira leads to symptoms of uraemia. Five drawings of sections of the infected kidneys are reproduced.

The second paper again describes the Utrecht disease. Mention is made of a guineapig which died 5 days after inoculation with 2 cc. of blood from a dog. In sections of the liver leptospira were demonstrated.

C. M. W.

HOFFMANN (W. H.). Zur Epidemiologie der Weilschen Krankheit. [**Epidemiology of Weil's Disease.**]—*Deut. Med. Woch.* 1927. Oct. 14. Vol. 53. No. 42. pp. 1781–1782. [Finlay Lab., Habana, Cuba.]

Assuming that both yellow fever and Weil's disease are caused by leptospira which produce in both very similar pathological changes it is surprising that epidemiologically they are so different. Weil's disease occurs in small outbreaks but yellow fever in large epidemics. Even during yellow fever epidemics cases of Weil's disease occur, and they persist when the yellow fever epidemic ceases. The presence of cases of Weil's disease in association with stegomyia does not lead to further cases of yellow fever. It seems evident that Weil's disease is dependent upon the infection in rats. These facts indicate clearly that the two diseases are completely independent of one another.

C. M. W.

GAY (Douglas Merrill) & SELLARDS (Andrew Watson). **The Fate of *Leptospira icteroides* and *Leptospira icterohaemorrhagiae* in the Mosquito,** *Aëdes aegypti.*—*Ann. Trop. Med. & Parasit.* 1927. Oct. 10. Vol. 21. No. 3. pp. 321–342. With 1 diagram. [19 refs.] [Harvard Med. School, Boston, Mass.]

With a view to throwing light on the relationship of *Leptospira icterohaemorrhagiae* and *L. icteroides* experiments were instituted to test the relative behaviour of these organisms in the yellow fever mosquito, *Aëdes aegypti.* The two strains employed were virulent to guineapigs so that it was possible to test the survival of the leptospira in the mosquitoes not only by direct examination of the crushed mosquitoes by dark ground illumination but by inoculating them into guineapigs. Furthermore, attempts were made to transmit the organisms from guineapig to guineapig and *L. icteroides* from guineapig to three human volunteers under conditions which have been proved necessary for mosquitoes to transmit yellow fever to man. The experiments were carefully controlled, all possible fallacies being avoided, the number of mosquitoes used being adequate. The outcome of the experiments is that there was no difference between the two organisms as regards their behaviour in the mosquito, and neither was transmitted by their bites. After ingestion from the blood of infected young guineapigs, the leptospira in the mosquito diminished rapidly in numbers

in the first few days, then more slowly till they eventually disappeared. In exceptional instances they survived in small numbers for three weeks during which they retained their virulence as demonstrated by inoculation of guineapigs. They thus diminish in numbers as micro-organisms in an unsuitable host would do. The observations furnish additional proof of the identity of *L. icterohaemorrhagiae* and *L. icteroides*.

C. M. W.

SELLARDS (Andrew Watson). **The Relation between Weil's Disease and Yellow Fever.**—*Ann. Trop. Med. & Parasit.* 1927. July 22. Vol. 21. No. 2. pp. 245–259. [21 refs.] [Harvard Med. School, Boston, Mass.]

This very interesting paper reviews the present position of yellow fever in its relationship to Weil's disease and the organism *Leptospira icteroides* as the author sees it as a result of his recent serological studies. The general conclusion is that the two diseases are fundamentally different in their etiology, epidemiology and pathology. The organism *L. icteroides* is not the causative organism of yellow fever and prophylactic immunization with it can give only a false sense of protection. If the serum of a patient convalescent from an acute infectious jaundice gives a positive Pfeiffer test with leptospira, using either *L. icterohaemorrhagiae* or *L. icteroides*, then yellow fever can be excluded and a diagnosis of Weil's disease can be made with justification.

C. M. W.

PUNTONI (V.). Rapports entre *Leptospira icteroides* (Noguchi) et *Leptospira icterohaemorrhagiae* (Inada et Ido). [**Relation of** *Leptospira icteroides* **to** *L. icterohaemorrhagiae.*]—*C.R. Soc. Biol.* 1927. May 6. Vol. 96. No. 14. pp. 1139–1141.

——. Studio dei rapporti fra la "Leptospira icteroides" (Noguchi) e la "Leptospira icterohaemorrhagiae" (Inada ed Ido).—*Ann. d'Igiene.* 1927. May. Vol. 37. No. 5. pp. 261–273. [16 refs.]

The paper describes in detail a series of serological and cultural investigations conducted with a strain of *Leptospira icteroides* (Palmeiras) and one of *L. icterohaemorrhagiae* (Pasteur Institute, Paris). The result is that morphologically, culturally and biologically, the two cannot be differentiated.

C. M. W

INADA (Jun). Ueber die chemische Zusammensetzung der Leber bei den experimentellen Spirochaetosen. [**Chemical Composition of the Liver in Experimental Spirochaetosis.**]—*Proc. Imperial Acad. Japan.* Tokyo. 1927. Mar. Vol. 3. No. 3. pp. 175–176. [Prof. R. Inada's Med. Clinic, Imperial Univ., Tokyo.]

The author has investigated the chemical changes in the liver of guineapigs infected with *Leptospira icterohaemorrhagiae, L. icteroides* and *L. hebdomadis.* Similar changes are produced by all three organisms, but they are less marked in the case of the last-named.

C. M. W.

FUKUSHIMA (Banji) & HOSOYA (Seigo). **A Study on the Culture Media of Spirochaeta. The Relation between the Life Phenomenon of the Spirochaeta and the Oxygen Tension and Cysteine, and the Culture Medium of *Spirochaeta pallida* supplemented by Cysteine.**—*Scientific Reports Govt. Inst. Infect. Dis.* Tokyo. 1926. Vol. 5. pp. 151–169. [27 refs.]

Culture experiments were carried out with *Treponema pallidum* and various strains of *Leptospira* in order to determine whether the organisms required aerobic or anaerobic conditions. The organisms were grown in anaerobic jars in media with or without fresh animal tissue or cysteine. All the strains of leptospira including those of Weil's disease, yellow fever, " Nanuka-Yami," " Akiyami " and water grew in the jars if tissue were present. They were thus proved to be definitely aerobic. On the other hand *Treponema pallidum* was definitely anaerobic and would grow in the presence of cysteine without fresh tissue.

C. M. W.

BROWN (H. C.) & DAVIS (L. J.). **The Adhesion Phenomenon as an Aid to the Differentiation of Leptospira.**—*Brit. Jl. Experim. Path.* 1927. Oct. Vol. 8. No. 5. pp. 397–403. With 2 text figs. [16 refs.] [Wellcome Bureau of Scientific Res., London.]

It has already been shown that under the influence of specific sera trypanosomes are altered in such a way that minute particles such as blood platelets or bacteria become adherent to them. In the present paper the authors have applied the reaction, which they call the adhesion phenomenon in place of the more cumbersome and less generally applicable term thrombocytobarin, to the differentiation of strains of leptospira. Specific sera were prepared by inoculating animals with strains of water leptospira (*Leptospira biflexa*), rat leptospira (*L. icterohaemorrhagiae*) and human leptospira (*L. icterohaemorrhagiae*, *L. icteroides*, *L. hebdomadis*). The various strains fall into three groups, *L. biflexa* group, *L. icterohaemorrhagiae* group including *L. icteroides* (5 strains), and *L. hebdomadis* group. It thus appears that the water leptospira (3 strains) form a group by themselves and are distinct from those which are parasitic in rats and human beings. Of the latter the Japanese *L. hebdomadis* (1 strain) is distinct from *L. icterohaemorrhagiae* and *L. icteroides* which appear to be identical. This result is in accord with the conclusions recently reached by other investigators who have shown that serologically (agglutination, Pfeiffer's reaction, etc.) *L. icteroides* is not to be differentiated from *L. icterohaemorrhagiae*. The authors have noted that the serum of apparently normal rabbits may show the adhesion phenomenon with strains of water leptospira. It is suggested that anti-bodies have resulted from ingestion of water leptospira by the animals. The sera of 100 wild rats were examined. Of these 32 reacted positively with the human and rat strains, 4 with both these and a water strain and 7 with a water strain alone. This is in accord with the natural infection rate of rats with *L. icterohaemorrhagiae* as given by STEVENSON in London (30 per cent.) and BUCHANAN in Edinburgh (36 per cent.).

C. M. W.

KRITSCHEWSKY (J. L.) & LEBEDEWA (M. N.). Untersuchungen ueber die genetischen Beziehungen bei den Spirochäten vom Typus icterogenes (Leptospirae) mittels der Thrombozytobarine. [**Genetic Relations of the Leptospiras as shown by Thrombocytobarin.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1927. Nov. 14. Vol. 53. No. 3-4. pp. 315-332. [15 refs.] [Educ. Commissariat, R.S.F.S.R., Moscow.]

Employing the thrombocytobarin reaction or adhesion phenomenon with various strains of leptospira—*L. icterohaemorrhagiae, L. pseudo-icterogenes, L. hebdomadis* and *L. icteroides* the authors have found that they can be differentiated by the use of immune sera prepared in mice. The number of organisms to which platelets adhered in each preparation was estimated and, recording the results as all, nearly all, a half, a third or none, it was found that races of the same organism showed differences. Occasionally the inoculation of a mouse for the production of immune serum produced lysins which prevented the serum being used for the test as it destroyed the organisms.

C. M. W.

HERRMANN (Erika). Serologische Untersuchungen bei Spirochäten vom Typus Weil. [**Serological Researches on Spirochaetes of Weil Type.**]—*Cent. f. Bakt.* I. Abt. Orig. 1927. Vol. 104. No. 1-4. pp. 192–194. [3 refs.]

The object of the paper is to draw attention to the serological changes which can occur in strains of leptospira. Two main types can be recognized—the non-pathogenic water type and the pathogenic types from rats and human beings. Not only do these two types differ from one another serologically, but the various strains of each type show serological differences. Such, however, are not constant, as they may be altered by culture in different media or passage through animals. Thus, in testing stock cultures it was found that two pathogenic strains (Berlin and Zaandam) which were originally serologically quite distinct had now become serologically reversed in dilutions of serum in 1 in 20. Similarly a water strain (Erlangen) after maintenance in Ringer's solution had ceased to be affected by an originally specific serum. Two strains (Berlin and Holland) had been induced to grow in media containing their own specific sera. With this Berlin strain a new immune serum in the rabbit was produced which agglutinated the organism in a dilution of 1 in 20,000, whereas it affected the original strain in only 1 in 200. The original strain was agglutinated by its own serum in 1 in 32,000. In another direction similar changes occur. The water strain Erlangen was successfully inoculated to guineapigs and after several sub-inoculations produced death with characteristic lesions. On two occasions strains of leptospira were isolated from these animals (strains 221 and 144). Immune sera prepared with these were specific, showing that the two strains differed from one another while neither strain was influenced by the original Erlangen serum. Testing the influence of the sera of 150 normal wild rats on the growth of 4 water strains, 2 yellow fever strains and 9 pathogenic strains, it was found that the water strains grew well, the yellow fever strains would not grow, while the pathogenic strains refused to grow in 15 per cent. of the sera. Another series of wild rats were inoculated with a strain pathogenic to guineapigs and it was found that 15 per cent. resisted infection. This

suggests that 15 per cent. of the Freiburg rats harbour a true Weil's strain. The conclusion is reached that the serological characters of leptospira are very labile and that the production of immune sera in rabbits is too delicate to be employed as a practical means of differentiating them. Rats again are able to respond by the production of different kinds of antibody.

C. M. W.

VAN THIEL (P. H.). **Leptospira Pseudoicterogenes.**—*Nederl. Tijdschr. v. Hyg. Microbiol. en Serol.* Leyden. 1927. Vol. 2. No. 1. pp. 70–84. With 2 figs. on 1 plate. [19 refs.] [Inst of Trop. Med., Leyden.]

Experiments with cultures of water leptospira have shown that, contrary to the views expressed by KABESHIMA (this *Bulletin*, Vol. 24, p. 712), it is possible for the organisms to pass through an L_3 filter when the added control bacteria do not pass. The method was to dilute with tap water 3 cc. of a 3 days old culture in 15 per cent. serum water. After this fluid has passed through the filter a little water is allowed to pass. If this precaution is not taken a negative result may be obtained. Filtration at pressures of 20 cm. to 70 cm. applied gradually or suddenly were equally effective. By this means pure cultures were obtained while further purification was secured by commencing cultures from single individuals. This was effected as follows :—Some of the filtrate in a very much diluted culture was taken. Very small drops were spread on a slide without a cover glass, and examined by dark ground illumination with low magnification. When a drop was secured which contained only a single leptospira the fluid was sucked up with the aid of some culture fluid into a small tube which was incubated at 37° C. It was inspected after a few days. These experiments were conducted some hundreds of times, and it was noted that a culture was never obtained unless a leptospira had been seen in the original drop of fluid examined. Though the fluid always contained innumerable granules none of these was able to give rise to a culture. It would appear therefore that a filterable granule stage of leptospira is excluded. It was shown that *Leptospira icterohaemorrhagiae* was able to pass as readily through the filters as the water leptospira. So far cultures of this organism have not been commenced from a single individual. In the serum water (15 to 20 per cent.) medium the water leptospira grows more readily than the rat leptospira while the reverse is the case with Noguchi's semi-fluid agar serum haemoglobin medium. There appeared to be definite morphological differences between the two organisms as grown in these culture media. The water leptospira were uninfluenced by a Weil's disease serum, or the serum of rabbits immunized against the human and rat strains. Though the water leptospira were rendered non-motile by an anti-Weil serum this was not a specific reaction as normal serum gave the same result. The water strain though it has been cultivated for nearly two years has never shown any inclination to become pathogenic to guineapigs or mice, while it has retained its serological distinctness from the human and rat strains. It does not appear therefore that age of culture has much influence in bringing about the change to pathogenicity of an original non-pathogenic water strain as UHLENHUTH and ZUELZER, who have noted such a change, maintain. There would seem to be a possibility that, when these observers noted a change to pathogenicity of a water strain, they were

dealing with a culture which, though obtained from water, contained both a water leptospira and a rat one also owing to the water having been polluted previously by rats.

C. M. W.

WALKER (John E.). **Leptospiras from Tap Water.**—*Jl. Infect. Dis.* 1927. Aug. Vol. 41. No. 2. pp. 164–168. [7 refs.] [Army Med. School, Washington, D.C.]

The author has confirmed HINDLE's finding that a culture of leptospira can be obtained from water by adding a small particle of faeces to some of the water in a Petri dish. In about 14 days a culture is obtained. He has also found that various substances can be used in the place of faeces, viz., hay infusion, broth, milk, egg, serum and blood. It was noted that in the case of faeces no growth was obtained if this were sterilized before adding it to the water, but that if a loopful of a culture of *Bacillus coli* were mixed with it growth occurred. The water used was Washington tap water which is practically free from this organism. Very good results were obtained with the following medium: Egg yolk, 1 cc., agar, 1 gm., tap water, 300 cc. The agar was dissolved by heat and when cool enough to handle, the egg yolk was added, the mixture being shaken. The medium while still liquid was poured into Petri dishes (20 to 30 cc. each). Each dish was inoculated with about 5 cc. of another culture. For the initial culture from tap water 1 cc. yolk was added to 300 cc. of tap water and then sufficient melted agar to give a 0·3 per cent. solution. The initial culture was always inoculated with *B. coli* though this did not seem to be so necessary when egg in place of sterile faeces was added. In this medium at room temperature leptospira developed in 4 to 10 days, reaching a maximum of 10 to 100 per microscopic field in 14 days. About 50 guineapigs were inoculated with cultures of the water leptospira but no infection occurred nor was there any evidence of latent infections. When *L. icterohaemorrhagiae* and *L. icteroides* were inoculated to this medium no growth occurred though survival for 10 to 30 days occurred. Subculture invariably failed. There was thus a marked contrast between the pathogenic and non-pathogenic strains.

C. M. W.

BAUER (J. H.). **A Method for the Isolation of Leptospiras from Water.**—*Amer. Jl. Trop. Med.* 1927. May. Vol. 7. No. 3. pp. 177–179. [5 refs.]

A method is described for isolating leptospira from water in West Africa. The water is filtered through filter paper, then through a Berkefeld V and finally through a Berkefeld N filter. A quantity (200 cc.) of the filtered water is mixed with 20 cc. of 2 per cent. nutrient agar melted and cooled to 45° C. and 2 to 3 cc. of fresh defibrinated guineapig blood. The mixture is then distributed in a number of test tubes (about 7 cc. to each) and kept at room temperature (22° to 35° C.) in the dark. A visible growth as a grayish haze was clearly seen between the 6th and 10th day if leptospira was present in the water. One or more of the tubes would be found to contain pure cultures. Rabbit's blood did not give such satisfactory results.

C. M. W.

BRILL. Zur Aetiologie des Schlammfiebers. [**Aetiology of Mud Fever.**] —*Muench. Med. Woch.* 1927. Sept. 9. Vol. 74. No. 36. pp. 1537–1540. With 3 curves & with 1 text fig. in Vol. 74. No. 43. p. 1858. [9 refs.] [Med. Univ. Polyclinic, Hamburg–Eppendorf.]

The paper gives a further account of the disease "Schlammfieber" or mud fever (see this *Bulletin*, Vol. 24, p. 712). Attention is directed to the general resemblance of the malady to Weil's disease. It is stated that a spirochaete-like structure was found in the blood. It was submitted to various people who agreed as to its spirochaete nature, but thought it unlike any known spirochaete. A microphotograph of the organism given in the second note is not entirely convincing. On the assumption that the disease was spirochaetal in nature, field mice were examined and it is claimed that spirochaetes were seen in smears of the heart blood and kidneys. The suggestion is made that the disease is contracted from water which has been polluted with spirochaetes by the field mice.

C. M. W.

CARPI (Umberto). Contributo alla conoscenza della spirochetosi ittero-emorragica nostrale. [**Icterohaemorrhagic Spirochaetosis in Italy.**]—*Riforma Med.* 1927. July 25. Vol. 43. No. 30. pp. 700–704. With 1 text fig. [16 refs.] [Ospedale Maggiore, Milan.]

A description of a case of Weil's disease which was diagnosed by the infection of guineapigs inoculated with the urinary sediment of the patient.

CUSHING (E. H.). **Leptospirosis Icterohaemorrhagica.**—*Jl. Amer. Med. Assoc.* 1927. Sept. 24. Vol. 89. No. 13. pp. 1041–1043. [4 refs.] [Bellevue Hosp., New York.]

The paper describes two sporadic cases of leptospiral jaundice in the United States. The organisms were recovered by inoculation of guineapigs from the urine of both cases and from the cerebrospinal fluid of one.

CERRUTI (C.) & REITANI (V.). [Ricerca della spirocheta ittero-emorragica nei ratti di Torino.] [**Spirochaetosis Icterohaemorrhagica in the Rats of Turin.**]—*Minerva Medica.* 1926. Vol. 6. No. 20. 2 pp. [Summarized in *Bull. Inst. Pasteur.* 1927. Aug. 15. Vol. 25. No. 15. p. 678.]

A record of the failure to discover *Leptospira icterohaemorrhagiae* in 100 *Mus decumanus* captured in various parts of Turin at different times of the year.

SCHÜFFNER (W.) & SIEBURGH (G.). Over de vroegtijdige microscopische diagnose van leptospirosen (Weilsche ziekte, gele koorts e.a.). [**Early Microscopical Diagnosis of Leptospiral Infections.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1926. Vol. 66. No. 6. pp. 801–806. [12 refs.]

A German version of this paper has been reviewed (this *Bulletin*, Vol. 24, p. 709).

C. M. W.

YELLOW FEVER.

i. GOUZIEN (P.). L'endémicité de la fièvre jaune en Afrique Occidentale. [**The Endemicity of Yellow Fever in West Africa.**]—*Rev. Méd. et Hyg. Trop.* 1927. July–Aug. Vol. 19. No. 4. pp. 97–108. [7 refs.]

ii. LEGER (Marcel). Spirochétose sanguine de l'Ouest-Africain. A propos de la communication de P. GOUZIEN sur la fièvre jaune. —*Ibid.* pp. 109–112.

i. This is a long and carefully reasoned argument in support of the view that yellow fever is actually endemic in West Africa. It was written by the first author, who has since died, as a reply to the criticisms of LAURENT (see this *Bulletin*, Vol. 24, pp. 101–103), who expressed the opinion that cases diagnosed as yellow fever in West Africa showed undoubted signs of malaria which had not been properly excluded. Attention is drawn to the probability of the disease existing in a modified form in the natives, to the possibility of the virus surviving in the mosquito during its period of hibernation, or of small mammals acting as reservoirs. A warning is issued against the confusion of yellow fever with blackwater fever, the differential features of the two diseases being emphasized. The conclusion is that yellow fever exists in French West Africa, and that it has numerous endemic foci. Its diagnosis presents no serious difficulties, but confusion with alcoholism, malaria and blackwater fever should be guarded against. Medical officers should constantly keep in mind the necessity of notifying every case of yellow fever so that all the means available for preventing the endemic disease developing into an epidemic may be immediately applied.

ii. The author of the second paper expresses his agreement with all that General GOUZIEN has written. He calls attention to the danger of giving quinine to yellow fever cases, a danger which has been generally admitted by many who have had to deal with the disease. He notes the reference to the possibility of there being a small mammal reservoir of the virus and details his own observations on the occurrence of a spirochaete of the relapsing fever type, *Spirochaeta crocidurae*, in small rodents of Dakar where relapsing fever in man occurs. The spirochaete of the rodents is inoculable to laboratory animals and to man and it would seem that the rodents may actually be playing the part of reservoir for a relapsing fever virus. If so, it has yet to be determined how the spirochaetes pass from these reservoirs to human beings and whether they represent a type distinct from those which are now well recognized.

C. M. Wenyon.

ROUBAUD (E.). La fièvre jaune dans le monde et les méthodes modernes d'action contre ce fléau. [**Yellow Fever and Modern Methods of Combatting it.**]—*Matériaux pour l'Etude des Calamités.* 1927. Apr.–June. Vol. 4. No. 13. pp. 50–74. With 4 maps. [13 refs.]

This is an interesting account of yellow fever from the point of view of its past and present distribution throughout the world and the methods which have proved useful in its eradication.

C. M. W.

JUNIOR (Vianna). Febre amarella. [**Yellow Fever.**]—*Brasil-Medico.* 1927. June 11. Vol. 41. No. 24. pp. 578–583. [2 refs.]

The paper describes six cases of yellow fever, three of them fatal, which were treated in the Isolation Hospital of Mont Serrat, Bahia. The chief interest lies in the isolation in Noguchi's medium of a leptospira from the blood of one of the fatal cases during May, 1926.

C. M. W.

MACKENZIE (Ian). **Notes on a Case of Yellow Fever.**—*Jl. Trop. Med. & Hyg.* 1927. Sept. 1. Vol. 30. No. 17. pp. 218–219.

Details of the clinical picture and post-mortem findings in a fatal case of yellow fever seen by the author in Sierra Leone in August, 1918.

C. M. W.

FOWLER (James K.). **"West African Yellow Fever."** [Correspondence.]—*Brit. Med. Jl.* 1927. Nov. 12. pp. 896–897.

This letter is written to call attention to an error which is sometimes made in referring to "West African Yellow Fever" as if it were a disease distinct from yellow fever. Reference is made to the paper by KLOTZ and SIMPSON reviewed below in which the authors, after the examination of tissues of thirty-five fatal cases from Nigeria and the Gold Coast, concluded that no fundamental difference was noted between the African disease and yellow fever.

C. M. W.

i. KLOTZ (Oskar) & SIMPSON (Winifred). **Jaundice and the Liver Lesions in West African Yellow Fever.**—*Amer. Jl. Trop. Med.* 1927. Sept. Vol. 7. No. 5. pp. 271–278. [9 refs.] [Dept. of Path., Univ. of Toronto, Canada.]

ii. —— & ——. **The Spleen in West African Yellow Fever.**—*Amer. Jl. Path.* 1927. Sept. Vol. 3. No. 5. pp. 483–488. [9 refs.] [Path. Labs., Univ. Toronto, Canada.]

i. The pathological study of material from 35 fatal cases of yellow fever from Nigeria and the Gold Coast leads the authors to conclude that no fundamental difference is to be noted between the disease as it occurs in Africa and America [a rather different conclusion to that reached by AITKEN and SMITH (this *Bulletin*, Vol. 24, p. 717)]. Yellow fever of West Africa is characterized by degenerative lesions in the liver, kidney and heart associated with haemorrhagic processes in the stomach, duodenum, skin and serous membranes and by endothelial response with degeneration in the spleen. There was variation in the fat deposits in the liver and kidneys. The authors draw attention to the fact that much of the difficulty in diagnosis of yellow fever from the point of view of the pathologist is the improper fixation of autopsy material, and the autolytic changes which progress rapidly in the damaged organs.

The lesions of greatest constancy were in the liver, so that it may be stated that yellow fever does not occur without damage to this organ. The toxin appears to have a selective action on the liver cells, which suffer degeneration and necrosis without any accompanying inflammatory process, as noted long ago by COUNCILMAN and ROCHA LIMA. They undergo an acidophilic and hyaline change, particularly in the mid-zonal region of the lobule. This change is present in some degree

in every case of yellow fever, whether jaundice occurred or did not occur during life. Though there is this intense destruction of liver cells the stroma of the lobule is unaffected, as also the vascular endothelial cells which line the sinuses of the lobules, even when the entire parenchymatous contents of the lobule are degenerated. Thus with intact sinuses, haemorrhage into the parenchymatous areas is seldom seen. Hyperplasia of the endothelial cells of the sinus, as described by SEIDELIN and TURNBULL, was noted. This affects the Kupffer cells, which may project as triangular or ellipsoid cells into the blood spaces. The Kupffer cells may show fatty degeneration which is sometimes marked. At other times they are acidophilic and granular while they may exhibit phagocytosis of red cells, lymphocytes and debris. The variation in the degree of damage to the Kupffer cells suggests an explanation of the variations in the extent of the jaundice. Though they may suffer intense degeneration and even exfoliation in the sinuses they are never completely necrotic. At the same time, there is injury to the endothelial system of the spleen and lymph nodes. It seems evident that there is serious damage to the whole reticulo-endothelial system which plays an important part in the production of bile pigment. If the liver cells are only moderately affected by the toxin there is hyperplasia of the endothelial cells which manufacture bile pigment with consequent well marked jaundice. On the other hand when early intoxication is intense and there is little or no jaundice, it is possible to demonstrate severe injury not only of the liver cells, but also of the endothelial cells which are inhibited as regards the formation of bile. When such severe cases recover, jaundice may appear during convalescence, an indication of the more early recovery of the endothelial cells. The pathology of the liver in cases of yellow fever thus lends support to the view that the reticulo-endothelial system is the important factor in bile pigment formation.

ii. In the literature dealing with the pathological changes in the internal organs in yellow fever very little reference is made to the spleen, which is usually unaltered in size and macroscopic appearance. On close examination of 35 cases from West Africa, the authors have found that the spleen suffers in a manner sufficiently distinctive to be of diagnostic value.

Microscopic study shows that the sinusoids of the pulp are widely dilated and engorged, while the pulp tissue itself shows evidence of polynuclear leucocytic infiltration only in those cases in which a hyperplasia of the endothelial cells is followed by their necrosis. The endothelial cells are crowded along the borders of the dilated sinusoids and only rarely is there evidence of their hyperplasia in the pulp areas. They show some phagocytic activity. More definite and constant changes occur in the lymphoid follicles, which macroscopically may appear either more prominent than usual or blurred and rather diffuse in their periphery. The normal follicle has a collection of endothelial cells at its centre and a sprinkling of these cells through the main lymphoid mass towards the periphery. The early reaction in cases of moderate intensity is the enlargement of the follicle brought about by hyperplasia of the endothelial cells. This is followed by diminution in size through loss of lymphocytes which disappear entirely from the spleen structure. Frequently this leads to a disappearance of many of the follicular masses in the place of which remain patches of endothelial cells, but when this stage has arrived there is evidence of endothelial degeneration.

Associated with the loss of lymphocytes from the malpighian bodies the endothelial cells in their peripheral portion and in the contiguous pulp become more prominent. They are larger and more numerous than normal, and are arranged along the border of the vascular spaces or are loosely attached to the neighbouring reticulum. Some, however, are free and show no relation to the fixed structures. These endothelial cells vary in size while some are spherical and others elongated and distorted. They are phagocytic and may show granular or hyaline degeneration. In later stages the endothelial cells at the centre of the malpighian bodies show hyaline changes and fusion of their structures. At the periphery of the bodies the degeneration is not of this type though they show a primary enlargement and granular degeneration followed by death and formation of debris. These changes often lead to the appearance of multinucleate forms and irregular fragments which are partly phagocytosed by the neighbouring reticulo-endothelium. Abnormal mitotic figures appear in some of the cells, indicating apparently a nuclear response in a degenerating cell. Furthermore the degenerating nuclei give rise to peculiar chromatin masses which may be mistaken for protozoan parasites. These changes in the spleen contrast markedly with those in the liver and kidneys where the parenchymatous cells alone suffer necrosis, the endothelial cells, though undergoing fatty degeneration, escaping complete destruction. The only reference to changes in the spleen in yellow fever similar to those described above is that of TURNBULL* who reported on two cases for the Yellow Fever Commission, in 1915.

C. M. W.

* *Yellow Fever Bureau Bulletin. Yellow Fever Commission (West Africa). Reports on Questions connected with the Investigation of Non-Malarial Fevers in West Africa.* 1915. May 29. Vol. 1. pp. 196–206.

MALARIA.

LEAGUE OF NATIONS. Health Organisation. **Principles and Methods of Antimalarial Measures in Europe. Second General Report of the Malaria Commission.**—95 pp. With 26 figs. (8 maps) & 3 charts. C.H./Malaria/73. 1927. July. Geneva.

JAMES (S. P.). **Problems of Malaria Prophylaxis. Conclusions of the Malaria Commission of the League of Nations.** *Brit. Med. Jl.* 1927. Aug. 27. pp. 340–343. Discussion pp. 343–344. [2 refs.]

The Second General Report on the Principles and Methods of Antimalarial Measures in Europe is dedicated to Dr. Norman v. LOTHIAN, Dr. Samuel T. DARLING and Mlle. A. BESSON who died so tragically when on duty on Lebanon. The collective study tours undertaken by the Commission have for the first time enabled malariologists of different countries and of different schools of thought to study local malaria problems on the spot. Individual views have thus become modified, and the final conclusion reached is in most cases a compromise —an average opinion which probably approaches the truth.

Rarely can there be any question of converting a malarious into a non-malarious place, an alteration which can be effected only by such a complete change in the character of a site as has occurred in course of centuries in London and Rome. In the Panama Canal Zone, the locality has not been essentially altered; malaria is merely being held in check and, were protective measures to cease, it would at once become devastating. Only very exceptionally then is it wise to aim at more than a significant reduction in malaria, one, however, which will suffice to make it of little or no importance as a cause of sickness and death. As regards the means by which this may be accomplished, the startling, yet on consideration correct, statement is made that there are localities where hardly anything has retarded the effective control of malaria so much as the belief that, since mosquitoes carry the infection, the elimination of these pests should be the object of chief concern and expenditure. It is on the contrary the case that in England, the Netherlands and Denmark malaria was robbed of its importance at a time when there was no knowledge of its epidemiology and no reduction of mosquitoes, and the Commission has seen exactly the same thing in process of happening in Europe to-day.

Of the actual measures which may be employed for the lessening of malaria, there is none of which it can be said that it is the method of unquestioned choice. That selected in any instance, after adequate local inquiry, must depend on local conditions. Yet such measures do fall into two great categories designated direct and indirect, the terms being, however, used in rather special senses. The direct measures of the Commission are those which kill malaria parasites, either in man through the treatment of infected persons, or in anopheles by the destruction of malaria-infected mosquitoes in houses. In the opinion of the Commission these direct measures are primary and always indispensable; the others though often most valuable are really adjuvant. The old aim of breaking the chain somewhere is, then, replaced by the new one of killing the parasites themselves. Nor is it held advisable that too many different measures of control should be put into operation at the same time; it is better to take one or two and carry them out thoroughly, for experience has enabled the laying down

of the valuable principle that for every measure there is a " minimum effective degree of perfection " ; if it be not carried out with a certain degree of thoroughness it is of no use at all.

Regarding the destruction of plasmodia in man by treatment it is pointed out that quinine, quinidine and kinetum are nearly equally effective in dosage of 1 gm. daily, while cinchonine falls into the same category if the dosage be increased to 1·5 gm. Quinidine is, however, the strongest cardiac depressent. Kinetum consists almost entirely of residual alkaloidal bases, the composition of the samples issued for these tests being quinine 15, cinchonidine 35, cinchonine 25, quinidine 5, and quinoidine 20 per cent. It must be concluded then that a standard preparation of the principal alkaloids, purified only so far as to exclude the more toxic constituents, is as efficacious as quinine. This conclusion implies that the " cinchona febrifuge " of India and Java regains its old eminence, always provided that it can be standardized. It also implies that the use of these total alkaloids in place of quinine only, greatly enlarges the amount of specific antimalarial alkaloid which is at present available for world use, and should, apart from commercial rings, correspondingly cheapen the cost of treating malaria. Moreover, the demand for, and so the cost of, cinchona alkaloids will be further reduced by the Commission's further pronouncement that " prophylactic quinine " in the usual preventive doses does not prevent malaria, it merely keeps in a certain abeyance an infection which has become established. In those ways more and cheaper alkaloid will become available for use where its action is most greatly to be desired. All this implies the primary importance of diagnosis, and the Commission indicates administrative methods by which its accuracy can be forwarded.

Regarding the similar direct attack upon plasmodia in anopheles, the procedure advised starts from the fact that, at least for Europe, the majority of infected mosquitoes are found inside houses, and that it is impossible to exaggerate the importance of their destruction there. Certain hospitable housewives offer within their homes to *Anopheles maculipennis* the attractive luxuries of cobwebs, dirt, dark corners and shady cupboards. They, and those who live with them, should be brought to regard the presence of gorged, sluggish, probably infective mosquitoes in the home much as cultured people now regard the bedbug and the louse, and to destroy them, or at least to put them to all possible discomfort by house cleaning and whitewash. Moreover, the Commission is satisfied of the usefulness of the suggestion, associated particularly with the name of ROUBAUD, that a damp dark still animal house situated between a breeding ground and the home will divert the insects to a harmless vicarious meal.

Regarding indirect antimalarial measures—during all the journeys of the Commission in different countries, only two regions have been found where large-scale antilarval measures have been definitely successful, in the Karst Mountains of Dalmatia and in parts of Palestine. In both, water is extremely scarce, strictly localized, and readily controlled. A return is made to the subject of Italian bonification, which signifies all work carried out with the object of making regions, which are periodically or permanently marshy, more suitable for agriculture and more healthy. This established value does not lie in the fact that they are essentially antilarval, indeed in many instances they actually increase, by means of their drains, the total area available for anopheline breeding. They are essentially social ; they change,

that is, a poor, sparse, scattered, often seminomadic population into one settled, well-to-do, aggregated into villages with schools, doctors, water supply, proper sewage disposal, and houses of an enforced hygienic standard ; and with this change malaria is lessened.

Finally the great need of continued research in malaria is made a matter of emphasis and a Section is devoted to the matter. The conveyance of malaria in the natural way by mosquitoes in this country, when infection is desired for the treatment of general paralysis, and not by the unnatural means of injection of infective blood in general use elsewhere, has enabled English workers to make certain valuable and unique observations.

These observations, together with an account of work in the Netherlands, Roumania, and Italy are embodied in the report, and the whole forms one of the most stimulating publications on malaria that has appeared in recent years.

Clayton Lane.

BOLETIN DEL INSTITUTO DE CLÍNICA QUIRÚRGICA. Buenos Aires. 1927. Vol. 3. Nos. 21–25. pp. 511–677.—**VIII. Paludismo.** [Also issued as *3a Reunión Soc. Argentina Patol. Regional del Norte, Tucumán. Julio, 7, 8 y 10, 1927.* pp. 403–584.]

One hundred and eighty pages in this large volume deal with malaria. Nelson C. DAVIS and collaborators go into the question, raised by the League of Nations Malaria Commission, and advocated by S. P. JAMES in Europe and Le PRINCE in Panama. of stressing the attack on adult mosquitoes in houses. They believe that it will be of value as a supplement to other measures, but their returns show that 183 anopheles were captured in 2,600 houses visited involving 892 hours' work. [It has apparently been overlooked that the Commission has aimed at getting the measures in houses adopted by the housewife ; few communities would tolerate these domiciliary visits by outside authorities.]

An interesting case is described by SPANGENBERG of chronic malaria with a " eunuchoid " condition in a person of 26 years, the genitalia being male and undeveloped with a penis 4 cm. long and the pubic hairs of the female distribution, but the face, axilla and front of the chest were hairless ; the mammae were developed, knock-knees and delicate bones present. The connexion with malaria is, naturally, difficult to establish but the case is of interest.

DOMÍNGUEZ publishes a valuable survey of the production of cinchona and quinine and points out that regarding cultivated trees the world supply of quinine comes from Java and India in the proportion of about 10 to 1, and urges that the cultivation of cinchona is for the Argentine not a problem to be studied but a work to be carried through. The plantation of cinchona on a profitable scale in its own natural home is merely a question of trial. Emilio FORTÉ considers methylene blue in quartan malaria, not as a substitute for quinine but as a drug to be used when there is " quinine resistance." Stovarsol by mouth in doses of 1 gm. daily for 4 days with 5 day intervals to a total of 16 gm. is advocated for pregnant women with tertian malaria by ETCHECOPAR, though he, as well as FORTÉ, has used the sodium salt. Dr. MAZZA and others have tried plasmochin, and plasmochin and quinine. Their conclusions are that the mixed drugs are useful in subtertian malaria, particularly against crescents, that the pure drug is effective in tertian and quartan infections and that it is without taste or secondary effects.

C. L.

McKenzie (A.). **The Distribution of Malaria in Dar-Es-Salaam.**—*Kenya & East African Med. Jl.* 1927. Sept. Vol. 4. No. 6. pp. 164–178. With 5 graphs & 1 map.

A spleen survey indicates that malaria is being conveyed by anopheles breeding in creeks which nearly surround Dar-Es-Salaam on the landward side. The spleen rate varied from 36·1 to 66·7 but the organ's size bore no relation to the local infection rate. The seasonal wave of malaria follows an increase in anopheline breeding, mainly it is believed in casual water near the houses of malarial patients, and it is concluded that the incidence of the disease will be favourably affected if these be controlled, even if the more permanent breeding grounds are untouched.

C. L.

Schwetz (Jacques). L'aspect entomologique de la lutte contre la malaria à Elisabethville. [**The Entomological Aspect of Anti-malarial Measures at Elizabethville.**]—*Bruxelles-Méd.* 1927. Aug. 14. Vol. 7. No. 42. pp. 1333–1339.

The Director of the Stanleyville laboratory, having collected or reared 35 species of mosquitoes in a year at Elizabethville, the brilliant capital of Kátanga with its beautiful avenues, numerous motors and fashionable ladies, comments energetically on the fact that there is nevertheless no hygienic service there, properly so called. Mosquito breeding places are—rejected jam jars found everywhere, ditches, dug out hollows, marshes, streams and rivers.

The anopheles caught and bred are—*A. costalis*, *A. funestus*, *A. implexus* (*chrystyi*) in one spot only, *A. mauritianus* ; those caught only —*A. pharoensis*, *A. wellcomei*, and *A. theileri* ; and those reared only *A. maculipalpis*, *A. squamosus*, *A. pitchfordi*, *A. transvalensis*. The common ones are *A. costalis* and *A. funestus*. But [it is very significant that] although *A. funestus* has frequently been caught, it has only been bred once. [Evidently its breeding places have hitherto eluded detection.] The need of a proper, independent, health service, under a competent and energetic medical man directly responsible to the Governor is insisted upon.

C. L.

Ledentu (G.) & Vaucel (M.). L'index du paludisme à Brazzaville. [**Malaria Index at Brazzaville.**]—*Bull. Soc. Path. Exot.* 1927. Oct. 12. Vol. 20. No. 8. pp. 722–726. [Pasteur Inst., Brazzaville.]

At Brazzaville in French Equatorial Africa the splenic index under 5 was 19·22 (312 cases), from 5 to 10 was 18·34 (327 cases) and from 10 to 15 was 10·09 (535 cases) ; for the different sexes it was 12·53 for boys and 11·48 for girls. The parasite index for the same age periods was 37·16 (600 cases), 26·39 (538 cases) and 16·36 (672 cases). Amongst 475 children *P. falciparum* was present in 33·89 per cent., *P. vivax* in 50·94 per cent., *P. malariae* in 4·63 per cent. and unidentified forms in 10·5 per cent. Gametocytes were present, in plasmodium positive cases, in the following percentages : *P. falciparum* 14·9, *P. vivax* 11·15

and *P. malariae* 13·6. Of those showing parasites, 22·2 per cent. showed enlarged spleen and 77·8 per cent. showed none; while of those not showing parasites the figures were 12·6 and 84·4.

C. L.

CRAWFORD (T. S. B.). **An Outbreak of Malaria in H.M.S. Daffodil.**—*Jl. Roy. Nav. Med. Serv.* 1927. Oct. Vol. 13. No. 4. pp. 309–311.

Crawford reports 25 cases of malaria contracted at Lagos among 95 white ratings. Plague inoculation seems to have been instrumental in precipitating attacks which, it seems, were being held up by prophylactic quinine. It seems then inadvisable to stress the long incubation periods which occurred. In 20 cases diagnosis was by the microscope, the Leishman stain having to be made up fresh since otherwise it rapidly lost its staining properties.

C. L.

ROSS (Ronald). **Malaria-Control in Malaya and Assam. A Visit of Inspection, 1926-7.**—31 pp. [Ross Institute & Hosp. for Trop. Dis., Putney Heath, London, S.W.15.]

This pamphlet constitutes the report of a visit of inspection whose general expenses were met by the Indian Tea Association, and is meant for lay readers. It is not intended to contain any new scientific observations but it lays a wise emphasis on certain aspects of the malaria problem. "Both malaria and malaria-control cost money; but the former costs health and even life itself." In addition—"It would be a 'profitable charity' for planters' managers to make their coolies employ [mosquito nets]." A planter's most practical test of his expense caused by malaria is his loss of labour and the sickness in his household during the malaria season. In his visits to Gibraltar, Malaya and Assam Ross dealt with points familiar to readers of this *Bulletin*. In Calcutta he had the pleasure and satisfaction of being present when Lord Lytton, Governor of Bengal, unveiled the handsome Gate of Commemoration leading to the little laboratory in the grounds of the Calcutta General Hospital where Ross worked out in 1908 the life cycle of *Plasmodium praecox* in sparrows.

C. L.

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1926.** [HOFLIN (J. W.).]—13 pp. 1927. Kuala Lumpur.

Regarding rice fields, the same conditions favour the growing of healthy rice and the breeding of healthy mosquitoes, the latter being those which normally breed in marshes. It is felt that the danger from rice fields is less than that from marshes since the anopheles have to recolonize the fields each year. The anopheline population varies. *A. sinensis* with some *A. barbirostris* may accompany the crop; or *A. fuliginosus* may predominate in young paddy with *A. aconitus* appearing near harvest time, or again both these last may flourish just before harvest. As a larvicide in wells petrol has been used in the strength of 3 ounces to 10 square feet of area. There has been immediate destruction of all larvae at a cost of 15 cents for a well of 8 sq. ft. of surface, the

water being potable in 3 hours and unspoilt for domestic use. The Board follows the example of Social Hygiene enthusiasts and advertises in the press under, for example, the heading "Why risk it?" which advocates a daily or regular hunt in the house and garden for anopheles adults and larvae.

C. L.

BOREL (M.). Résultats d'une enquête épidémiologique et entomologique à la plantation de Gia-Nhan (Cochinchine). [**An Epidemiological and Entomological Inquiry in a Cochin-China Plantation.**]—*Bull. Soc. Path. Exot.* 1926. Oct. 13. Vol. 19. No. 8. pp. 677–680.

An account of the miserably malarious state of a plantation situated in the midst of virgin jungle in Cochin China. It employs 162 coolies, and although 45 of them are married there is not a child younger than 10 years in the place and the few children above that age are pitiful objects. The predominant parasite is *P. vivax*, which in a few instances was associated with *P. malariae* and once with *P. falciparum* also. The only Anopheles (larvae) found there were *A. maculatus* and the ubiquitous (and probably innocuous) *A. vagus*.

A. A.

UNITED STATES NAVAL MEDICAL BULLETIN. 1927. Oct. Vol. 25. No. 4. pp. 1017–1020.—**An Epidemic of Malaria at the United States Naval Station Olongapo, P.I.**

Of the 47 cases infected, 22 admitted to having been in the native city of Olongapo after sunset 2 to 3 weeks preceding the attack. The prevalent wind blew from this part to the anchored ships. The subtertian parasite was identified in 34 cases, the tertian in the rest. The latter responded to quinine promptly, the former tardily. Prophylactic quinine was not given, deliberately and after full consultation.

C. L.

MALARIACOMMISSIE VOOR NOORDHOLLAND. Jaarverslag der Wetenschappelijke Malaria-Commissie voor Noord-Holland over 1926. [**Annual Report for 1926 of the Scientific Malaria Commission for North Holland.**]—[ALDERSHOFF (H.), Chairman, KORTEWEG (P. C.), Secretary.]—35 pp. [19 refs.] 1927.

The last report, with references to former ones, is found in this *Bulletin*, Vol. 23, p. 811. In 1926 anopheles larvae were first reported on April 14th, probably a fairly normal date for Holland, since the similar dates for other years lie between April 3rd and May 4th. The first males were found in Amsterdam on June 2nd, females having as usual been found in stables throughout the whole year, smallest numbers being collected in June (53) and largest in October (2,100).

For the destruction of larvae, Paris green and paraffin have been compared. In the laboratory 10 cc. of a 1 per cent. mixture of Paris green in dust per square metre of water surface has killed all anopheles larvae, which eat it as it floats on the surface. It has no influence on pupae [which do not feed] nor on culex larvae [which are not surface feeders], nor on anopheles larvae which are put into a tank 24 hours after the application of Paris green [by which time it has sunk]. In the field

the same strength of Paris green per square metre kills all or nearly all larvae even when the spot is strongly infested. If there be a strong breeze blowing a larger quantity of the poison must be used. No ill effects were observed on fish. As regards the choice between Paris green and paraffin the former acts well in wide stretches of water with local vegetation, but since it harms neither pupae nor egg, so that small larvae are already to be found 3 days after its application, it has to be used about twice as often as paraffin—in Holland every fortnight.

The attack upon the imagines has included the destruction in Amsterdam of over 4,000,000 in stables and 2,841 in 260 houses where malaria had been present. The aim is propaganda to get householders to undertake the destruction of all mosquitoes which force their way into dwellings.

Of suspected blood films examined in Amsterdam 29 per cent. were positive, practically the same as in the previous year, and, as before, the incidence of malaria in certain medical practices is considered, while the annual admissions to provincial hospitals since 1921 are compared with those of 1901. The numbers for 1901 being 48 and for the years from 1921 onwards 11, 50, 13, 20, 36, 31.

Investigating the liability to relapse, 27 cases which had been treated for malaria in 1925 were examined by thick drop preparation in February or the beginning of March, 1926. No parasites were found, but 7 of them fell ill again with malaria in 1926, 4 of them during May, and these, it is held, may reasonably be considered as relapses. In another series of examinations a person sick with malaria in 1925 and thoroughly treated, and found negative to the thick drop on April 16th, May 14th and June 1st, fell sick with malaria on June 25th.

Regarding the value of screening, figures are given suggesting that 3 times as many infections occur among those who are unscreened as compared with those who use screened bedrooms. Regarding anopheline races the maxillary dentation does not follow the lines suggested by MARTINI.

C. L.

SLIWENSKY (M.). Die Malariafrage in Bulgarien. [**Malaria in Bulgaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Sept. Vol. 31. No. 9. pp. 414–428.

Long before the Great War malaria was a scourge in Bulgaria, comprising a quarter of all admissions to hospital. All three species of parasite are involved and the anopheles found are: (1) *Anopheles maculipennis* and *A. elutus*, those mostly implicated. They are found to a height of 1,400 metres [about 4,500 feet] and breed in swamps, wells and water in gardens; so that both adults and larvae are domesticated. (2) *A. bifurcatus* is very rare but occurs with *A. maculipennis* in ricefields. *A. pseudopictus* is wild, not found in houses or stables and breeding in ricefields. *A. superpictus* shares with *A. maculipennis* a wide distribution in the Struma valley corresponding with its presence in Macedonia and Thrace. The spleen rate runs as high as 50 per cent. One village, during the last ten years, has had 148 births and 250 deaths, and the yearly monetary loss to the country is estimated as 100,000,000 lei. Since the War the usual antimalarial prophylactic measures have been carried out.

C. L.

TRACHONIOTOVSKY. Le paludisme sur le territoire occupé par la République Allemande du Volga. [**Malaria in the German Republic of the Volga.**]—*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 7. French summary p. 469. [In Russian pp. 422–426.

The district comprises three zones—steppe, riverine and hill. The malarial sick in 1925 and in the first eight months of 1926 were respectively per 1,000, 577·4 and 296 in the steppes, 925 and 373·5 in the riverine zone, and 201·1 and 141·6 in the hills.

C. L.

MARGINESU (P.). [Le paludisme à Sassari (Sardaigne) : étude statistique et épidémiologique des années 1924, 1925 et 1926.] [**Malaria at Sassari, Sardinia.**]—*L'Igiene Moderna.* 1927. June–July. Vol. 20. Nos. 6 & 7. pp. 174 & 196 [Summarized in *Bull. Office Internat. d'Hyg. Publique.* 1927. Sept. Vol. 19. No. 9. pp. 1324–1326.]

By the aid of the dispensary, " Emiciclo Garibaldi," and the application of petroleum, Paris Green and gambusia to [different parts of] the 17,000 square metres of breeding places which surround Sassari, the malarial morbidity in Sassari has fallen from 167 in 1924 to 88 in 1925 and 58 in 1926. The quarters benefiting most are those nearest to the treated breeding places, but malaria has been contracted throughout the town. The epidemic period extends from June to December or January. Parasites were found in 76·5 per cent. of cases judged to be malarial; the specific percentages among the positives being *P. vivax* 52·7, *P. falciparum* 43·1, *P. malariae* 1·8, mixed infections 2·2. The spleen rate is given only for cases diagnosed as malaria, and is not therefore comparable with that of other places.

C. L.

MISSIROLI (A.) & HACKETT (L. W.). La regressione spontanea della malaria in alcune regioni d'Italia. (**Spontaneous Regression of Malaria in some Regions of Italy.**)—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 193–243. With 6 text figs. [Refs. in footnotes.] [English summary p. 491.] [Anti-Malaria Exper. Station, Italy.]

" In four regions of Italy noted for the gradual but complete disappearance of malaria during the past century the authors, by numerous observations and experiments, have measured the extent of the contact of *A. maculipennis* with man. They confirm in general the conception of ROUBAUD and WESENBERG-LUND that the transmission of malaria has ceased because of a change in the habits of this mosquito which causes it to seek as a host stabled domestic animals to the virtual elimination of man. This change seems to be an inherited adaptation amounting to specificity in the parasitic relationship between *A. maculipennis* and domestic animals. The factors underlying such development in the habits of the insect are the great adaptability of this particular species and the progressive stability of the agricultural population which has led to the continuous stabling of the many domestic animals. In contrast with other regions, Europe has but one very domesticable anopheline, *A. maculipennis*, and the course of malaria has accompanied the stages of adaptation of this species, appearing when the mosquito began to enter

the habitations of man, and disappearing when it abandoned these for the more favourable environment of the continuously-occupied stable.

"Merely to surround human dwellings with stables or pigsties does not reproduce at once the conditions which obtain in regions of anophelism without malaria. The necessary adaptation develops *slowly*, but becomes the decisive factor in the actuation of a complete spontaneous regression of malaria."

C. L.

FALLERONI (Domenico). Per la soluzione del problema malarico italiano. (Bonifica agraria e zooprofilassi. Battaglia del grano—risicoltura). (**The Solution of the Malaria Problem in Italy.**)—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 344–409. [English summary p. 493.] [Anti-Malaria Station, Pontine Marshes.]

A. claviger [*A. maculipennis*] is a house mosquito with definite preferences and will use human habitations or animal houses according as either sort is attractive in position, numbers or conditions. It acts as a vehicle for infection just because it is domestic. It will mature its eggs up to 8 or more days after a blood feed. Zoophile races of anopheles were not observed but stress is laid on the proper siteing of animal houses in human prophylaxis.

C. L.

FRANCHINI (Giuseppe). Brevi note di malariologia in provincia di Bologna. [**Notes on Malaria in Bologna Province.**]—*Arch. Ital. Sci. Med. Colon.* 1927. May. Vol. 8. No. 5. pp. 246–252. [Inst. Trop. Path., Univ. Bologna.]

This paper is mostly of local interest. In confirmation, however, of the findings of GRASSI and others that *A. pseudopictus* is a bad transmitter of malaria as compared with *A. claviger* [*maculipennis*], it is noted that in localities where malaria was endemic and least infrequent all anopheles found were *A. claviger*, where malaria was rare *A. pseudopictus* became commoner, and where it was absent their numbers were increased.

C. L.

OTTOLENGHI (D.). in collaboration with BROTZU (G.), LA FACE (L.), BRIGHENTI (D.) & ROBUSCHI (L.). Intorno all' azione esercitata dalle bonifiche sull'endemia malarica nel Ferrarese. (**On the Action of the Agrarian Sanitation Works on the Malaria Endemics of the Ferrarese.**)—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 268–343. With 10 figs. (4 maps). [Refs. in footnotes.] [English summary pp. 492–493.] [Anti-Malaria Exper. Station, Italy.]

In localities investigated *A. maculipennis*, *A. elutus*, *A. pseudopictus* and *A. bifurcatus* have been found. The first two are important but unequally distributed, the second being numerous where malaria exists,

rare or absent where malaria has disappeared. *A. elutus* appears to have the greater preference for human dwellings. No relationship was traced between malaria and social and economic conditions.

C. L.

CARR (Henry P.) & CLARKE (J. Lyell). **A Study of the Incidence and Distribution Characteristics of Malaria in Rural Areas of Southern Illinois.**—*Amer. Jl. Trop. Med.* 1927. July. Vol. 7. No. 4. pp. 251–268. With 2 maps. [6 refs.] [Illinois State Dept. of Pub. Health, Springfield & Intern. Health Board, Station for Field Studies in Malaria, Edenton.]

Diagnosis was primarily by examination of the spleen in the supine position with thighs sharply flexed and clothing opened, the examiner palpating the skin. Deep breathing was used. Of the 1,500 boys examined between the ages of 2 and 12, 171 had enlarged spleens, 161 or 94·1 per cent. being palpable only on inspiration ; of the remaining 10, 7 were " palpable," one reached one finger's breadth and two 3-fingers' breadths below the costal margin. The situation of the home of every child examined was marked on a large scale map. The terrain consists of river valleys at a level of 300 feet to 400 feet and a more hilly region running up to 800 feet. The spleen index of the former was 14, of the latter 3·7. In two towns it stood at 4·4 and 7·3. Malaria then, it is concluded, constitutes a major public health problem in this part of the state. Even in the hilly parts it forms a not insignificant malaria rate, taking as normal the 1 per cent. London figures of ROSS, CHRISTOPHERS and PERRY. There has been found, too, a definite relationship in the same child between the occurrence of splenomegaly, and chills and fever. To the decline in malaria of recent years there is widespread testimony.

C. L.

BARBER (M. A.), KOMP (W. H. W.) & HAYNE (T. B.). **The Susceptibility to Malaria Parasites and the Relation to the Transmission of Malaria of the Species of Anopheles Common in Southern United States.**—*Public Health Rep.* 1927. Oct. 14. Vol. 42. No. 41. pp. 2487–2502. [44 refs.]

After a critical consideration of the evidence to be found in the many references cited the writers draw the following conclusions :—

" The three species of *Anopheles* common in southern United States, *A. quadrimaculatus*, *A. punctipennis* and *A. crucians*, are all easily infected with malaria parasites in the laboratory. All have been found infected in nature, *A. quadrimaculatus* and *A. crucians* with sporozoites in the salivary glands. *A. punctipennis* has been proved capable of transmitting malaria to man under laboratory conditions. *A. quadrimaculatus* is the summer species of widest distribution. It is the one most commonly found in dwellings and has been found infected in nature in higher proportion than the other species. Epidemiological evidence goes to show that it is the most important carrier of malaria in southern United States. In any antimosquito malaria control work this species should receive first attention, but we do not believe that the evidence thus far adduced can exculpate either *A. punctipennis* or *A. crucians* as possible carriers of malaria. "

C. L.

DAVIS (Nelson C.), CABARROU (Félix C.) & LAINO (Fernando). Estudios entomológicos en su relación con la lucha antipalúdica. [**Entomological Investigations in Connexion with the Anti-Malarial Campaign.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1927. Vol. 3. Nos. 21–25. pp. 733–743. With 2 charts. [3 refs.] [Also issued as *3a Reunión, Soc. Argentina Patol. Regional del Norte, Tucumán, Julio, 7, 8 y 10, 1927.* pp. 625–635 & illustrations.]

These investigations were undertaken by the National Department of Hygiene of the Argentine with the help of the Rockefeller International Board of Health. The object was to find out the prevailing malaria vectors in the Northern Argentine. The result of a large number of captures went to prove that *A. pseudopunctipennis* is the chief vector, but that *A. argyritarsis* plays no part; at all events the authors' results in respect of the latter were quite negative. *A. tarsimaculatus* and *A. albitarsis*, though incriminated owing to their prevalence at certain seasons of the year and their presence in the houses, are but suspects, the case against them being not yet proven.

H. Harold Scott.

SHANNON (Raymond C.) & DEL PONTE (Eduardo). Informe preliminar sobre los anopheles transmisores del paludismo en la gobernación de Misiones. OYARZABAL (Julio). Constatación protozoológica del paludismo en la gobernación de Misiones. [**Anopheles transmitting Malaria in Misiones, Argentina.**]—*Semana Méd.* 1927. Sept. 15. Vol. 34. No. 37 (1757). pp. 695–699. With 2 charts. [1 ref.] [Bact. Inst., National Dept. of Hygiene, Buenos Aires.]

This paper deals with mosquito distribution in various localities. Dealing widely, it is noted that the carrier of malaria in North West Argentine, where the rainfall is less than 1,000 mm. and the wet season between December and June, is *A. pseudopunctipennis* breeding in running or still water, and in pools formed by the rains, exposed to the sun, with abundant algae and an alkaline reaction. In Alto Paraná the rainfall is from 1,800 to 2,000 mm.; the carriers are *A. albitarsis* and *A. tarsimaculatus*, breeding occurring probably in the dry season which follows the heavy rains, in still spring water, exposed to the sun, without algae and with an acid reaction.

C. L.

BUTLER (C. S.) & PETERSON (E.). **Malaria in Haiti.**—*U.S. Nav. Med. Bull.* 1927. Apr. Vol. 25. No. 2. pp. 278–288. With 2 charts & 7 figs. on 4 plates. [2 refs.]

This reprint from the *Journal of the American Institute of Homeopathy* tells how Haiti, by malaria and yellow fever, defeated Napoleon in 1802 and is yielding now to more appropriate methods of pressure. Malaria, apart from control measures, is proportionate to the rainfall which varies greatly. The spleen index lies between 0·88 and 100. The low lying coastal plains abound in seepage springs and are dammed for rice cultivation, and there *A. albimanus* abounds. Covered subsoil drains and rectified surface drains have produced (according to corrected tables) marked benefit to health, and much reclaimed land which has enlisted the active interest of the farmers. Work continues.

C. L.

GILL (C. A.). **The Forecasting of Malaria Epidemics with Special Reference to the Malaria Forecast for the Year 1926.**—*Indian Jl. Med. Res.* 1927. July. Vol. 15. No. 1. pp. 265–276. With 1 map. [6 refs.]

Fourteen years ago Gill entered on the task of attempting to forecast malaria epidemics, an attempt which has been condemned by a Calcutta daily paper of wide circulation—" sickness being as much psychological as physiological." Gill has remained unperturbed by the possible psychological effect of his forecast either on the plasmodium or the patient. His view, put forward in 1924, is that malaria epidemics are the outcome of " loss of equilibrium " between " infection " and " immunity." There are five factors concerned in the forecasting of an epidemic flare up of malaria during October–November in the Punjab, and they fall into the two groups as follows. " Infection " is dependent on humidity at the right season, which experience shows to be measured in the Punjab by the July–August rainfall ; and on the anopheline population at the same season which in the Punjab has, however, been found to have no influence on the extent of malaria in October–November and is now ignored. " Immunity " depends on the spleen rate factor, the economic factor and the epidemic potential factor. The spleen rate factor is based on a census of 40,000 school children taken in June and November during the last 12 years. Its significance depends on the observation that epidemics of malaria of appreciable intensity never occur in localities in which the spleen rate, as compared with the previous five years, is absolutely and relatively high. It is noteworthy, then, that the spleen rate here is valued not as a measure of the risk of infection in which the community stands, but of the degree of temporary immunity which at the time it possesses. The economic factor is concerned with the average price of food grain, and the induction from analysis of statistics that economic stress may profoundly influence the magnitude of epidemic malaria. The epidemic potential factor is measured by " the co-efficient of variability of fevers " during October for the period 1868–1921. It is of value in that there is no need to anticipate an outbreak of malaria where none has occurred during 55 years, even if other factors are favourable for its occurrence. The District forecasts have had a large measure of success.

" To the writer it would appear that predictions which give a month's warning of the occurrence of an impending catastrophe are of considerable value, not only because they enable timely action to be taken to mitigate misery and distress, but because they permit of the inspiring hope that a quest embarked upon some 14 years ago is approaching its objective."

C. L.

BRUG (S. L.) & WALCH (E. W.). **Report of an Investigation of a Malarial Epidemic in Solo, 1926.**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1927. Part 3. pp. 531–579. With 2 folding plans & 8 figs. on 6 plates. [2 refs.]

A very full report is issued but with necessarily uncertain conclusions. That the outbreak was in actuality acute is indicated by a parasite index higher than the splenic index, by a close proximity between the parasite indices of adults and children and by a high percentage of crescent carriers (68 to 86 per cent. of subtertian infections) ; mortality reached as much as 54 per mille. The carrier was not

detected. The stomachs of about 600 anopheles and the salivary glands of 60 were examined. Only one infection was discovered, a single cyst in one stomach of an *A. rossii*. Much larger catches were, however, made in buffalo houses than in dwellings. The percentages were as follows:

	A. rossi.	*M. vaga.*	*M. aconita.*	*N. fuliginosus.*
Dwellings ...	35%	63%	1%	1%
Buffalo houses	3%	81%	2%	13%

Nevertheless a catch on one day "gave the surprising result that also *N. fuliginosus* appears to be sometimes a true philanthropist."

C. L.

COVELL (G.) & BAILY (J. D.). **Observations on Malaria in the Andamans; with Special Reference to the Enlarged Spleen in Adults.**—*Indian Jl. Med. Res.* 1927. Oct. Vol. 15. No. 2. pp. 309–326. With 4 charts. [11 refs.] [Central Malaria Bureau, Kasauli, India.]

The splenic apex has been noted in 825 cases in adults. Its path seems to follow that in children. The highest parasite index was associated with a splenic apex about 6·8 cm. from the umbilicus and 6·2 cm. from the costal margin or one of 3 to 4 finger breadths. The findings of SCHÜFFNER and CHRISTOPHERS are confirmed, namely that gamete output is not associated with immunization, but the reverse. Quartan malaria is unusually frequent, but the degree of splenic enlargement could not be associated with any plasmodium species. It is concluded that CHRISTOPHERS' method of splenic measurement is, with modifications, applicable in the field and gives far more accurate results than do those hitherto employed, and that SINTON's method of enumerating malaria parasites by a standard suspension of fowl's blood is convenient and easy of application in field conditions.

C. L.

MACKENZIE (Ian). **A Research into the Pathology, Prophylaxis and Treatment of Subtertian Malaria.**—*Jl. Trop. Med. & Hyg.* 1927. Aug. 15. Vol. 30. No. 16. pp. 205–208.

Over a period of 9 years Mackenzie has made a detailed examination of 1,150 cases of subtertian malaria with a view to investigating quinine prophylaxis, the causes of the changes in certain organs and the biological properties of the gamete. Of 627 new arrivals in the tropics, a third was given 5 grains of quinine prophylactically, a third iron and arsenic and a third no prophylaxis. Total relapses or reinfections after 3 months were 8·2, 9·5 and 13·2 per cent. respectively. It is held that there is a marked relationship between low blood pressure, decided anaemia and localization of symptoms, that when an attack occurs during quinine prophylaxis it is apt to be more intense and to react less readily to quinine than usual, and that the prophylactic dose must be raised to 10 grains daily when infected mosquitoes are numerous. The writer has examined thousands of films and hanging drop preparations in many malaria cases and has failed to find anything suggestive of retrogressive schizogony, that is "parthenogenesis." He has obtained sporulating subtertian parasites six times on splenic puncture when only crescents were visible in the peripheral blood. The shortest

time required for the disappearance of crescents from the peripheral blood smears under quinine treatment was 5 days, the average 17·5 and the longest 28 days.

C. L.

CHODUKIN (N. J.) & LISOWA (A. I.). Zur Frage ueber die Möglichkeit von Erkrankungen an Malaria im Winter. [**The Possibility of Malarial Infection in Winter.**]—*Pensée Méd. d' Usbekistane.* Taschkent. 1927. No. 6–7. German summary pp. 132–133. [In Russian pp. 76–89. With 6 figs. on 1 plate. 9 refs.]

There are, it is believed, two kinds of hibernating *A. elutus*, one with a fat-body, really hibernating; and one without, merely surviving. In a warm room the former can become active, the fat-body shrinking and the ovary developing. The writers have shown that these hibernating mosquitoes can become infected with *P. vivax* and *P. malariae*, that ookinetes can remain in the stomach for 8 days at a temperature of 2° to 8° C. and then develop to active oocysts, that oocysts survive a temperature of 0° to 8° C. for 30 days, or one of 8° C. maintained for not longer than 20 hours, and that sporozoits can live in the salivary glands for 30 days at 0° to 8° C. They conclude that *A. elutus* hibernating in houses can infect, and that winter and spring infections are to be attributed to it.

C. L.

COOGLE (C. P.). **The Spleen Rate as a Measure of Malaria Prevalence in the United States.**—*Public Health Rep.* 1927. June 24. Vol. 42. No. 25. pp. 1683–1688. [7 refs.]

About 7,000 school children have been questioned and examined with a view to obtaining positive information or evidence regarding malarial incidence, and the point is considered under the heads of history, spleen index and parasite index. The spleen index was obtained with the child standing, bending forward and deeply breathing, the blood examination by a thick smear. The history index was positive in 1,689 of 7,143 children or 24 per cent., the maximum being 61·9 in white children in Leflore County, Miss. and the minimum 7·4 in white children in Chatham County, Ga. The spleen index in 7,108 children was 4, with a minimum of 0·2 in coloured schools in Chatham County and a maximum of 15 in coloured children in Leflore County. The parasite index in 6,103 children averaged about 7, with a minimum of 0·9 in South Carolina, the children being nearly all white, and a maximum of 29·7 in white children in Taylor County, Fla. The low infection rate is attributed to the short period of transmission (mid June to end of September), an economic status which can afford food and quinine, and to the observation that " the disease has a definite trend downward in this country, already having disappeared from large areas."

C. L.

POPOV (S. P.) & SHAPSHEV (K. N.) [**The Question of the Transmission of Malaria by Lice.**] [In Russian.]—*Profilakt. Med.* Kharkov. 1925. No. 11. Reprint 4 pp. [Summarized in *Rev. Applied Entom.* 1927. June. Vol. 15. Ser. B. Pt. 6. p. 112.]

" In view of previous observations on lice as a reservoir from which mosquitos might become infected with malaria a series of experiments

was made. The lice (*Pediculus humanus*, L.) were allowed to feed on malaria patients and were then dissected at varying intervals after feeding. It was found that at 12–15° C. the gametes ingested by the louse begin to degenerate 1 hour after feeding, and that after 3–4 hours as a rule they have all been destroyed, apparently owing to the action of digestive juices. At 37° C. degeneration occurs sooner and is completed within 3 hours."

C. L.

BROWN (F. V. Bevan) & PULLON (E. Douglas). **A Case of Malaria contracted in New Zealand.**—*New Zealand Med. Jl.* 1927. June. Vol. 26. No. 133. pp. 119–123.

A man who had not left New Zealand, except to visit Sydney and Melbourne in 1914, developed fever after visiting Auckland and occupying a bed recently vacated by a man suffering from influenza. He had, in all, 12 attacks between June, 1925, and February, 1926, characterized in general by high fever without sweating, violent dry cough without sputum, moist sounds at the bases, a patch of impaired resonance below the left scapula, nothing abnormal to X-rays, but greyish pallor during the attacks. It was a fever with 7 to 13 days intervals and 4 to 5 days duration. During the 7th attack one film showed "two bodies which might have been intra-corpuscular B.T. rings," another "malarial stippling or something very like it." Next day a *thick* film showed "typical B.T. parasites and rings." Oral quinine hydrochloride, 30 gr. for 6 days did not stop the 8th attack, which was, however, milder than usual, half the quinine being given intramuscularly as soon as the attack matured. By now the "malaria parasites had evidently lost heart" and the attacks gradually ceased. No anopheles have ever been identified in New Zealand [It is noteworthy that a *thick* film showed "typical B.T. parasites and rings."]

C. L.

LJACHOWETZKY. Ueber angeborene Malaria. [**Congenital Malaria.**]—*Cent. f. Bakt.* I. Abt. Orig. 1927. Sept. 10. Vol. 103. No. 6-8. pp. 380–390. [Pasteur Inst. of the Crimea, Simferopol.]

It seems impossible to do otherwise than consider this paper critically. Several hundred mothers and children are dealt with in a series of tables, the age of the children varying from 1 day to 2 years. The close personal postpartum conditions in which mother and infant lie are those which favour the earliest possible transmission of malaria by anopheles from mother to child. Accordingly it is not reasonable to accept any case of malaria as congenital unless the infant is found to be infected within an interval from birth which is less than the shortest known incubation period of malaria. This criterion does not seem to be indisputably present in any of the cases dealt with in this paper.

C. L.

LIPSCOMB (F. M.) & MANSELL (R. A.). **A Case of Congenital Malaria.**—*Jl. Roy. Army Med. Corps.* 1927. July. Vol. 49. No. 1. pp. 44–48. [13 refs.]

Malaria parasites (*P. vivax*) were first found in thick film in the child when 26 days old, he having been born and since resident in Murree, Northern Punjab, with an altitude of 7,200 feet, a place where acquisition of malaria has never yet been reported. The child's fever began on the third day after birth and was tertian in type for 3 attacks.

C. L.

DOROLLE (P.) & DANG-HUU-CHI. Coma palustre et grossesse. Présence de *Plasmodium praecox* dans le sang du cordon. [**Presence of** *P. praecox* **in the Cord Blood in Pregnancy.**]—*Bull. Soc. Path. Exot.* 1927. July 13. Vol. 20. No. 7. pp. 589–591.

A woman 5 months pregnant died comatose. A hurried autopsy showed a very large soft spleen, kidneys congested with punctiform haemorrhages and with subcapsular ecchymosis of the left, pancreas with punctiform infarcts, the uterus with retroplacental haemorrhagic foci covering a area of about a 5-franc piece and with infarcts varying in size from a pin's head to a pea. Microscopically, the spleen showed rings of *P. falciparum*, sometimes two in one corpuscle, but no forms of other age and no gametocytes; pigment was abundant, free and in leucocytes. The blood of the cord showed schizonts and sporulating bodies of *P. falciparum*, much pigment, but apparently no gametocytes—at least they are not mentioned.

The rarity of congenital malaria is noted (this case was the only one in seven examined in which the condition was present) and its existence is explained by the placental haemorrhages which existed, with their antecedent vascular ruptures.

C. L.

TATE (D. Laurence). **A Case of Ruptured Malarial Spleen: Splenectomy with Recovery.**—*Lancet.* 1927. Nov. 12. p. 1020. With 1 text fig.

An enlarged spleen was ruptured in a fall from a buggy, chiefly on to the abdomen. The man vomited, had some abdominal pain, and passed two blood-stained stools. Thirty hours later he was first seen in a collapsed state, with a rigid painful tender abdomen, the tenderness particularly in the hypochondrium and right iliac fossa. A right rectus incision had to be abandoned, on entering the peritoneum, for a large one giving access to the splenic pedicle. This was tied and the spleen removed. Plentiful salines pulled him through, and he left hospital 4 weeks later. Four weeks later still, he reported complaining, not of malaria, but of gonorrhoea.

C. L.

DOROLLE (P.) & DAN HUU CHI. Rupture spontanée de la rate au cours d'une fièvre rémittente à *Plasmodium praecox*. [**Spontaneous Rupture of the Spleen in Subtertian Fever.**]—*Bull. Soc. Path. Exot.* 1927. Oct. 12. Vol. 20. No. 8. pp. 719–722. With 1 text fig. [1 ref.]

Of three prisoners shut up at night in a hospital at Hagiang, Tonkin, one died with the history that he had complained of intense cold, but never of pain. Death was from haemorrhage from an extensively ruptured spleen. *P. falciparum* was present in splenic smears.

C. L.

KARVE (S. D.). **Disorders of the Digestive System in Malaria.**—*Kenya & East African Med. Jl.* 1927. June. Vol. 4. No. 3. pp. 95–98.

Apart from nervous reactions, the disorders here considered are stomatitis, gastritis, diarrhoea and dysentery. The stomatitis is aphthous, very painful, very offensive by the fourth day, and occurs in children; the blood shows plasmodia in half the cases and clears up under quinine, "preferably by injections." Gastritis, diarrhoea and dysentery begin only when the temperature falls; the infection displayed is generally subtertian. The treatment found most effective for the last has been a combination of quinine and emetine.

C. L.

BASILE (G.). L'appendicite malarica? [**Malarial Appendicitis?**] —*Policlinico.* Sez. Prat. 1927. Aug. 8. Vol. 34. No. 32. p. 1143.

Commenting upon DEMJANOW's conclusion that malaria must be accepted as causing appendicitis (this *Bulletin*, Vol. 24, p. 263) BASILE draws attention to the well-known lesions caused by malaria parasites in which inflammation has no part. It is correct to speak of malaria simulating, but not of its causing, appendicitis, peritonitis or encephalitis. This mimicry, he notes, seems first to have been recorded by FORD (*Medical Record*, 1903), again by GILLOT (*Sem. Médicale*, 1905) and next by BASILE (*Bull. d. Soc. Lanc.*, 1906). He exclaims that there has been described of recent years a malarial epididymitis.

C. L.

URCHS (O.). Die Beziehungen der Malaria zum Nervensystem. [**Malaria in its Relations to the Nervous System.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Aug. Vol. 31. No. 8. pp. 365–375. [23 refs.] [Surinam Bauxite Co.'s Hosp., Moengo, Dutch Guiana.]

The cases observed fall into 3 series.

1. Damage to the peripheral nerves, including trigeminal neuralgia, associated with malaria parasites and clearing up under quinine.
2. Herpes zoster in 5 cases within 20 months associated, with parasites in 2, perhaps in 3, cases and clearing up under quinine.
3. Two fatal cases—one with blackwater fever and encephalitic foci at autopsy, the other showing leptomeningitis.

C. L.

DE VRIES (Ernst). **Nervous Complications in Pernicious Malaria.**—*China Med. Jl.* 1927. June. Vol. 41. No. 6. pp. 503–508. [8 refs.] [Peking Union Med. Coll., Peking.]

That the condition was malarial is based on the finding of crescents on spleen puncture, and later in cutaneous blood, after repeated negative findings, when the patient came under observation 6 weeks later. The main nervous symptoms were cerebellar ataxy, intention tremor, increased reflexes, slow and slurring speech, and non-convergence of the eyes. The Wassermann reaction was negative in blood and spinal fluid.

C. L.

VITUG (W.) & IGNACIO (P.). **Clinical Mimicry in Malaria.**—*Jl. Philippine Islands Med. Assoc.* 1927. Aug. Vol. 7. No. 8. pp. 275–282. [Coll. of Med., Univ. Philippines.]

The writers cite a number of cases illustrating the well-known protean character which the symptoms of malaria may take—influenza, typhoid, dysentery, uraemia, meningitis and cholecystitis being stimulated. The last is worthy of mention.

A death occurred in a man of 34 with fever, abdominal pain, often extremely acute causing him to cry out, deep jaundice, distended rigid tender abdomen, the last two symptoms particularly evident in the right upper quadrant. Liver and spleen could not be felt; no malaria parasites were found. "Autopsy revealed a normal gall bladder and no evidence of peritonitis. Acute splenitis and hepatitis due to malaria were the principal post-mortem findings."

C. L.

TORRES (C. Magarinos) & DE AZEVEDO (A. Penna). Sur l'hépatomégalie dans le paludisme. [**Hepatomegaly in Malaria.**]—*C.R. Soc. Biol.* 1927. Nov. 18. Vol. 97. No. 31. pp. 1358–1361. [Oswaldo Cruz Inst., Rio de Janeiro.]

In the attempt to determine whether enlargement of the liver accompanying malaria is attributable to vascular alterations or to the increase in size of individual lobules, the writers have counted the number of portal spaces visible per 100 sq. mm. histological sections 6 to 8μ thick—in acute malaria, in chronic congestions of the liver and in controls in whom the liver is apparently normal. The numbers have been, respectively, 37·7 the average of 13 cases, 44 the average of 11 cases, and 58·86 the average of 10. The portal spaces are, then, pushed further apart than normal and the lobule correspondingly increased. There is also fatty degeneration.

C. L.

MANSON-BAHR (Philip) & MAYBURY (L. M.). **The Association of Quartan Malaria with Nephritis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1927. Aug. 31. Vol. 21. No. 2. pp. 131–134. With 1 chart in text. [6 refs.]

Two cases of quartan malaria are described in which there occurred general oedema, albuminuria 1 to 1·5 per cent. and hyaline and granular casts. Under quinine no improvement occurred so long as parasites persisted in the peripheral blood, but as soon as these were disposed of, the general and renal condition showed improvement and each patient was discharged from hospital with no evident signs or symptoms of nephritis.

C. L.

PERUMAL (M. V.). **Indigenous Cases of Malaria at High Altitudes.**—*Indian Med. Gaz.* 1927. Oct. Vol. 62. No. 10. pp. 553–554.

Ten cases are reported where malaria appeared in persons who stated that they had never been at an altitude lower than 5,500 feet. Five had been in Coonoor since birth [latitude 11′ 20″ N.]. Eight of them harboured subtertian and six tertian parasites, so that there were four mixed infections. The quartan parasite was absent. The station consists of a series of ridges, over 6,000 feet in altitude, intersected by deep valleys running down about 500 feet. Half the cases occurred in Dhoby Ghat, where there is "continuous breeding of mosquitoes."

C. L.

KANDIAH (M.). **How to distinguish Albumen from Quinine in Mayer's Test.**—*Malayan Med. Jl.* 1927. Sept. Vol. 2. No. 3. p. 99. [Inst. Med. Research, Kuala Lumpur, F.M.S.]

If the upper part of a test tube containing urine which shows a precipitate to Mayer's test be heated, the precipitate due to quinine disappears on boiling—to reappear on cooling; while that caused by albumin becomes denser.

C. L.

VAN DEN BRANDEN (F.) & HENRY (E.). Nouvelle médication du paludisme par la plasmoquine. [**Treatment of Malaria by Plasmochin.**]—*Bull. Soc. Path. Exot.* 1927. Oct. 12. Vol. 20. No. 8. pp. 728–734. [7 refs.]

Plasmochin compound has been tested in three cases in which schizonts of *P. falciparum* were present and were not removed from the peripheral blood; and in two cases in which crescents were present and had disappeared after a course of treatment lasting two to four weeks or more. Regarding *P. malariae*, four cases were treated with plasmochin and one with plasmochin compound. In all of them, schizonts, segmenting forms, and gametocytes disappeared. This appears to be one of the first records of the effects of plasmochin compound on quartan malaria, the examinations being made every 6 days for 12 weeks, 12 weeks, 8 weeks, 6 days and 6 days.

C. L.

MAZZA (Salvador), FORTÉ (Emilio), ALVAREZ SOTO (Napoleón) & ARIAS ARANDA (Carlos). Nota preliminar sobre los efectos de la plasmoquina pura y plasmoquina compuesta en el paludismo. [**The Effects of Plasmochin and Plasmochin Compound in Malaria.**]—*Prensa Méd. Argentina.* 1927. Sept. 20. Vol. 14. No. 11. pp. 446–454. [10 refs.] [Univ. of Buenos Aires.]

In this appreciative paper, it is concluded that the immediate effects of plasmochin compound (plasmochin and quinine) in subtertian malaria are superior to that of any other treatment, and that it causes the disappearance of crescents in 4 to 6 days—one case has been followed for 7 months [others for 7 days]. Plasmochin itself, in appropriate doses, is equally efficient in tertian and quartan malaria. There is an absence of taste and of disagreeable after-effects which makes the drug particularly useful for children and for patients with a quinine idiosyncrasy.

C. L.

CHEREFEDDIN. Behandlung der Malaria mit Plasmochin. [**Treatment of Malaria with Plasmochin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Aug. Vol. 31. No. 8. p. 375.

The writer concludes after experience with three cases that the action of plasmochin on subtertian rings is stronger than is that of quinine and that on crescents it is very certain and good. In one of his cases which had four plasmochin tablets daily for 9 days, an injection of neosalvarsan and ice to the spleen produced a relapse of rings and rosettes which disappeared under a second course of plasmochin.

C. L.

ANTONELLI (Giovanni). La plasmochina nella cura dell' infezione malarica. (**Plasmoquin in the Treatment of Malaria.**)—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 414–434. [2 refs.] [English summary p. 494.]

"'Plasmoquin' (a new synthetic preparation obtained from quinoline) has given satisfactory results in 33 cases of different forms of malaria, and has shown itself specifically efficacious against the different types of parasite and the febrile manifestations. But the therapeutic results

are not permanent, especially in the cases of malignant tertian fever. In several patients the medicament causes a special cyanosis and some dyspeptic troubles, which do not represent a serious complication and generally disappear with the interruption of the treatment."

C. L.

UNITED FRUIT COMPANY, BOSTON, MASS. FIFTEENTH ANNUAL REPORT MEDICAL DEPARTMENT. 1926. pp. 66–71. [3 refs.]—**Experiences with Plasmochin in Malaria. (Preliminary Reports),**

A report had been sent by Dr. Wilhelm CORDES, of Preston Hospital, Cuba, on the use of plasmochin compound. In strict rotation he placed each of 72 patients entering hospital in two lists, odd numbers getting 2 gm. [30 grains] of quinine daily; and even numbers 8 plasmochin compound tablets daily, corresponding to 1 gm. of quinine [15 grs.] and 0·08 gm. of plasmochin. Crescents disappeared from the peripheral blood in from 3–7 days of quinine and plasmochin treatment except in one case, where they persisted for 8 days; of the quinine group, 11 had crescents on discharge from hospital. Toxic symptoms developed in 4 cases, with one death, and on them a separate communication is to be issued, pending which it should not be concluded that the death was the result of the plasmochin.

C. L.

FLETCHER (William) & KANAGARAYER (K.). **Plasmochin in the Treatment of Malaria.**—*Indian Med. Gaz.* 1927. Sept. Vol. 62. No. 9. pp. 499–506. [4 refs.] [Inst. Med. Research, Kuala Lumpur, F.M.S.]

"*The Advantages and Disadvantages of Plasmochin.*—The tastelessness of plasmochin and the absence of unpleasant symptoms after it has been swallowed, such as bitterness in the mouth, nausea, noises in the ear, deafness and amaurosis, are all points in its favour when compared with quinine. Its action in benign tertian malaria is equal to that of the cinchona alkaloids, and in quartan fever it destroys both trophozoites and gametocytes even more quickly. We have seen several cases in which relapses occurred after treatment, but the conditions under which our observations were made do not enable us to say whether they are more or less frequent than after treatment with quinine. Plasmochin appears to have the property of destroying the crescents of subtertian malaria, and this unique attribute suggests the possibility of ridding whole districts of malaria by mass treatment of the population. Unfortunately plasmochin has two great drawbacks; the first is the uncertainty of its action upon subtertian trophozoites and the second is its toxicity, which renders mass treatment impracticable. It must be administered under medical care, and those undergoing treatment should be examined daily, because toxic symptoms sometimes supervene with great suddenness. It would not be safe to issue it for sale to the general public or to supply it (as quinine is supplied in the Malay States) to police-stations and to local headmen for free distribution. It is not suitable for the treatment of gangs of labourers on railways or road-construction, where the actual administration of remedies is often in the hands of a native overseer. It is, in short, a drug more fitted for use in the hospital than for the outpatient."

These conclusions are based on the treatment of 97 patients.

C. L.

MÜHLENS (P.). Die Plasmochinbehandlung der Malaria. [**Treatment of Malaria by Plasmochin.**]—*Deut. Med. Woch.* 1927. Nov. 4 & 11. Vol. 53. Nos. 45 & 46. pp. 1891–1893; 1933–1936. [18 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

Mühlens sums up the recent literature on plasmochin. He remarks that as originally stated plasmochin removes the schizonts of tertian and quartan malaria, and plasmodium compound [which title is apt to disguise the fact that about one gramme of quinine is being taken daily] is equally valuable for subtertian malaria schizonts and crescents. It is further stated that this prompt and certain action on the parasites implies marked clinical results and that there are fewer relapses than with quinine; that blackwater fever and cases with "quinine idiosyncrasy" should be treated by the drug, that the young and weak bear it well. While admitting, contrary to his former report [this *Bulletin*, Vol. 24, p. 266] which was to the effect that the cyanosis accompanying plasmochin was an unaesthetic vasomotor effect of a neuropathic nature, that plasmochin produces methaemoglobin, he holds that there is no more risk from this in dosage of 0·01 gm. per 10 kilos body weight, than in the case of quinine or salvarsan. He agrees with CHEREFEDDIN that with plasmochin the treatment of and fight against malaria enters on a new phase.

C. L.

MANOLOFF-SLIVEN (S.). Erfahrungen ueber die Malariabehandlung mit Plasmochin. [**Plasmochin Treatment of Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Nov. Vol. 31. No. 11. pp. 518–523. With 3 charts in text.

The report covers 7 subtertian, 2 quartan and 1 tertian case. In the subtertian cases crescents disappeared, but quinine had to be called in to clear the blood of rings. In one of them after 7 days of 0·06 gm. plasmochin daily there occurred marked abdominal pain particularly epigastric, tenesmus, with incessant desire to defaecate and collapse. In the tertian and quartan cases all forms of parasites disappeared, but the period of observation is unnoted.

C. L.

FISCHER (O.) & WEISE (W.). Ueber Wirkungen und Nebenwirkungen des Plasmochins bei der Behandlung der menschlichen Malaria. [**Action and By-Effects of Plasmochin in Treatment of Malaria.**]—*Deut. Med. Woch.* 1927. Aug. 12 & 19. Vol. 53. Nos. 33 & 34. pp. 1380–1382; 1421–1424. With 7 charts in text. [13 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

All writers on the use of plasmochin as an antimalarial drug have noted the cyanosis which it causes. This Fischer and Weise cannot attribute to the heart, but have examined it from the point of view of methaemoglobinaemia.

Cases investigated were given 0·05 or 0·1 gm. plasmochin daily by injection for 6 or 7 days, and an after treatment which varied. In tertian and quartan malaria 0·05 gm. plasmochin was given orally twice daily for 4 consecutive days a week, the course lasting 5 weeks. In subtertian malaria, previous work having shown that relapse would very quickly follow, the after-treatment was by quinine, 1 gm. daily in 5 doses. Crescents disappeared in 2 to 7 (average 4) days, asexual

forms in 5 to 6 days, and fever in 24 to 48 hours. No relapses and no reappearance of crescents occurred within an observation period of 5 weeks, although in one case, where rings only were present at the beginning of treatment, crescents appeared on the thirteenth day.

Methaemoglobinaemia was measured in a layer of 5 per cent. blood 4 cm. thick, by which could be measured spectroscopically any quantity from 4 per cent. upwards. Of 26 patients tested daily for some weeks, methaemoglobinaemia was absent from one only, in the others it ranged from 4 to 20 per cent., the last in those getting 0·1 gm. daily in whom also " cyanosis " was so strongly marked that plasmochin had to be taken off and quinine substituted. Nevertheless the cyanosis might gradually disappear even though plasmochin was resumed. The earliest first appearance of methaemoglobinaemia was 24 hours after the first plasmochin injection and the last evidence was 10, indeed to a slight extent 12, days after the cessation of administration.

Certain experiments suggest that the greater the initial anaemia, the greater the induced methaemoglobinaemia. Investigation was then made with smaller doses of plasmochin. With a daily dose of 0·03 gm. 10 of 13 cases showed methaemoglobinaemia and with one of 0·02 gm. 7 of 17, the drug being continued for 7 days. With this dosage it is held that there is no risk; while, on the average, crescents disappear in 5 to 6 days with either daily quantity, and always within 10 days. With this small dosage schizonts, if present in the cutaneous blood, do not disappear from it, nor, it is held, is it to be expected that they should. The effect rather is that while crescents disappear rings multiply and a typical attack results which has to be cut short by quinine. The plasmochin acts; indeed, as a provocative. A case is cited where crescents were present in the blood. Under douching of the spleen, adrenalin and sunlight schizonts appeared. In spite of daily intramuscular injections of 0·02 gm. of plasmochin the attack became so serious that quinine had to be given, up to 1 gm. daily and 6 gm. in all. Crescents, however, appeared, again to disappear under plasmochin. An after treatment by quinine was begun. Two months later he relapsed with both schizonts and crescents in the blood. In yet another case crescents disappeared from the blood for 3 days under plasmochin, many schizonts persisting and quinine having also to be administered. Nevertheless crescents reappeared and persisted until, after an interval of 10 days, plasmochin was resumed. It is concluded that for the treatment of fresh attacks and for prophylaxis quinine should be combined with plasmochin.

C. L.

SLIWENSKY (M.). Der Gametenversuch mit Plasmochin in epidemiologischer Betrachtung. [**Gametes and Plasmochin: Epidemiological.**] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Nov. Vol. 31. No. 11. pp. 523–526.

In 81 cases treated with plasmochin compound, which means a daily dosage of plasmochin varying between 0·075 and 0·08 gm. and of quinine up to 1 gm. [15 grains], all three forms of malaria parasite were removed from the blood for 4 months when the treatment had been carried through for 6 days. There was no abdominal pain and no cyanosis, and the treatment is held to be practical and economical.

C. L.

VAD (B. G.) & MOHILE (G. B.). **The Place of Plasmochin in the Treatment of Malaria.**—*Indian Med. Gaz.* 1927. Aug. Vol. 62. No. 8. pp. 430–434. With 16 charts. [Sir J. J. Hosp., Bombay.]

The writers mention the two kinds of tablets in which the makers put up the drug plasmochin, 0·02 gm. recommended for tertian and quartan malaria and plasmochin compound containing 0·01 gm. of plasmochin and 0·125 gm. of quinine, advised for subtertian malaria and have treated all three kinds of malaria in 17 cases. They add, "all the cases under investigation were given only the tablets of the new drug and no other medicine whatever." It does not then seem clear whether they gave the simple tablets only, or acted as they say they did "according to the directions of the manufacturer" and gave the considerable doses of quinine contained in the compound tablets to subtertian cases. They have obtained very satisfactory results and add "The days of quinine are numbered. By virtue of its surpassing merits plasmochin has successfully challenged the place of quinine. Plasmochin is another triumph for German synthetic chemistry. It has no untoward or after effects." [Such enthusiasm is refreshing but scarcely borne out by the general experience.]

C. L.

HEGNER (Robert) & MANWELL (R. D.). **The Effects of Plasmochin on Bird Malaria.**—*Amer. Jl. Trop. Med.* 1927. Sept. Vol. 7. No. 5. pp. 279–285. [6 refs.] [Johns Hopkins School of Hyg., Baltimore, Md.]

"The experiments recorded above confirm and extend the results obtained by Roehl (1926) on the action of plasmochin on malaria in birds [see this *Bulletin*, Vol. 24. p. 264–5]. Daily doses of 1·5 mgm. given orally are effective, but are not easily tolerated by the birds. Heavy doses of 1·0 and 0·5 mgm. given daily for five succeeding days after a single inoculation prevent acute infections but do not prevent the appearance of parasites in the blood. Similarly smaller doses of from 0·07 to 0·2 mgm. given on five successive days after parasites appeared in the blood prevented acute infections but not the continuance of parasites in the blood. Daily small doses of plasmochin (0·1 mgm.) prevented the appearance of parasites in the blood of birds that were at the same time given daily inoculations of parasites. Plasmochin in doses of 0·1 mgm. for two weeks prevented the death of birds with acute infections that were deprived of large quantities of blood. The death of a bird suffering from a severe relapse was also apparently prevented by daily doses of 0·1 mgm. for two weeks. Plasmochin is thus shown to be a very effective therapeutic agent in bird malaria. It does not, however, destroy all the parasites in the body of the host and hence does not free the host from the possibility of relapse. On this account efforts should be continued to discover a drug that will destroy all of the parasites and hence prevent what is probably the greatest single factor in the spread of malaria—relapse."

C. L.

CARDAMATIS (Giovanni P.). La cura delle febbri malariche. [**Treatment of Malarial Fevers.**]—*Malariologia.* 1927. Aug. 15. Ser. 3. No. 2. pp. 21–27. [14 refs.]

This survey of the treatment of malaria follows orthodox lines and quotes largely from the opinions of others. Cardamatis's own treatment for an adult consists in the administration of 1·6 gm. [23 grs.] of quinine on the first day, divided into 2 doses given within an hour.

The subsequent daily dose for 11 days is 1·5 gm. 7 to 8 hours before the access. After a 4 days interruption a single dose of 1 gm. is given daily for 8 days. Administration is dropped for a week and resumed for two (*P. vivax*) or three (*P. falciparum* or mixed infections) months at the rate of 1 gm. daily, which may be omitted on one day in the week.

C. L.

NEVIADOMSKY (M. M.). Traitement de la malaria d'après la méthode de l'école russe. [**Treatment of Malaria after the Russian Method.**] —*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 6. French summary p. 336. [In Russian pp. 333–336.]

Failure in malarial treatment is attributable either to insufficient quininization or to a perfunctory examination of the spleen. So long as splenic enlargement persists infection persists, so that the technique of palpation requires close attention. The best treatment consists in the daily administration of 1·5 gm. of quinine hydrochloride in 5 fractional doses together with 30 injections of a 2 per cent. solution of arsenate of soda. In chronic cases, and after a month's course as above indicated, give twice a day 15 to 20 drops of [? tincture of] iodine, and if splenomegaly persist repeat the whole line of treatment till it disappears.

C. L.

ROSENTHAL (Georges). L'injection sucrée de quinine, formule moderne du traitement du paludisme. [**Malarial Treatment by Quinine in Sugar Solution.**] -*Rev. Path. Comp. et Hyg. Gén.* 1927. Sept. 5–20. Vol. 27. No. 332–333. pp. 946–949. [Pasteur Inst., Paris.]

Using intravenously, in 1918, LO MONACO's saccharose solution for maladies other than malaria Rosenthal was struck with the way in which the veins completely escaped injury after repeated injections, and has used it as a vehicle for quinine injection, as often as 25 times in a single person.

The solution is put up in ampoules according to one or other of these formulae.

(*a*)	Quinine hydrochloride or bihydrochloride	0·3 gm.
	Urethane	0·3 gm.
	Glucose solution 30 per cent., or	
	Saccharose solution, 30 to 100 per cent.	5 cc.
(*b*)	Quinine hydrochloride or bihydrochloride	0·5 gm.
	Urethane	0·3 to 0·5 gm.
	Glucose or saccharose solution as above	10 cc.

The dosage is 0·3 to 1·1 gm. daily, quinine being preferably given by mouth on alternate days.

The urethane is a quinine solvent, this last being apt to crystallize out of the hydrochloride solution unless the urethane is in quantity equal to the quinine. The 100 per cent. saccharose solution, given slowly, is preferred, but there may apparently be a nitritoid crisis if the total amount is as much as 20 cc. In diabetes, saccharose 30 per cent. should replace glucose. To avoid fainting the injection should always be given with the patient lying down. The use of two needles, one to draw the quinine into the syringe, and the other for injection,

so avoiding the presence of caustic quinine outside the needle is thought hardly necessary. The use of tincture of iodine for the skin is not insisted upon.

C. L.

BOULKINE (A. K.). Le paludisme et son traitement dans le district de Vilouisk de la République autonome de Yakoutsk. [**Malaria and its Treatment in the Vilyuisk District, Yakutsk Republic.**] —*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 6. French summary p. 382. [In Russian pp. 374–381.]

The author's résumé runs somewhat as follows :—

Tertian malaria has existed so long in Vilouisk that it may be held indigenous. For the first time it has been diagnosed by the microscope. Oral administration of quinine is impossible in such an uncivilized community; besides it produces quinine-fast organisms. Intravenous medication is the only rational treatment. It should be given in doses of 0·4, 0·3, 0·2 and 0·1 gm. at intervals of 10, 15, 20 and 30 minutes [the intervals should, however, be fewer by one than the doses], and is without inconvenience. The fractional dosage produces desensitization to quinine, is economical and should be the only prophylactic measure used, since those against imagines and larvae and for draining of marshes are inapplicable to local conditions.

C. L.

DARKER (G. F.). **Tetanus following Intramuscular Injection of Quinine.** [Correspondence.]—*Lancet.* 1927. Aug. 6. p. 306. [1 ref.]

"It always seems to me that the cause of tetanus after intramuscular injection of quinine is a rusty hypodermic needle. On the west coast of Africa where tetanus spores are common I have made many injections of quinine without mishap. I have used a platinum needle and have refused steel needles, because when once damp they always go rusty inside even if kept bright on the outside.

"There is another point. Intramuscular injection of a dense solution of quinine causes a necrotic nodule in goats and I have no doubt the same is produced in human beings. I therefore use bihydrochloride of quinine, one part dissolved in eight or ten of water."

[The suggestion that bihydrochloride of quinine in 10 to 12½ per cent. solution does not cause necrosis seems to be without support. Darker exercises great care in sterilization of solutions and instruments.]

C. L.

VAN NITZEN (R.). L'action du stovarsolate de quinine sur les infections à *Plasmodium falciparum.* [**Stovarsolate of Quinine in Subtertian Malaria.**]—*Bull. Soc. Path. Exot.* 1927. Oct. 12. Vol. 20. No. 8. pp. 727–728.

Stovarsolate of quinine was given in doses of 1·5 gm. daily to 23 adults, and a sixth to a third of that dose to 8 children. Crescents disappeared from the blood in 3 to 36 days in adults and 5 to 21 days in children. On the schizonts it had much less effect. In two these disappeared more rapidly than did crescents, in two equally rapidly, and in 21 less rapidly; indeed they have persisted after 30 to 43 gm. of the stovarsolate have been taken. SEGUIN is quoted as authority for

the statement that quinine in doses of 3 to 5 cgm. per kilo destroys crescents in 30 to 50 days. Plasmochin was given to 6 adults. The doses sufficient to remove crescents were 14 to 33 tablets [each containing 0·02 gm.] in 5 to 7 days—in one case 20 days. Schizonts were uninfluenced. "Circulatory troubles" were often provoked, while the stovarsolate was well supported and without ill effects.

C. L.

RAYNAL (J.). Essais de traitement des tierces bénigne et maligne par le stovarsolate de quinine. [**Treatment of Tertian and Subtertian by Stovarsolate of Quinine.**]—*Bull. Soc. Path. Exot.* 1927. July 13. Vol. 20. No. 7. pp. 665–689. With 10 charts in text. [Refs. in footnotes.] [Michel Lévy Hosp., Marseilles.]

Four cases of tertian malaria were treated with stovarsolate of quinine in three ten-day courses of 1 gm. daily, the courses separated by five-day intervals so that the whole occupied 40 days. In 3 of them relapses occurred 15, 18 and 41 days after the cessation of the last course, while in the fourth no relapse had occurred up to 47 days. The attacks themselves were rapidly controlled by the drug. Four cases of subtertian malaria were also treated, with rapid control. Crescents disappeared in 39, 31 and 16 days. There had been no relapses in 1, 3 and 4 months, the fourth man being repatriated and lost sight of.

C. L.

SINTON (J. A.), BIRD (W.) & EATE (S. N.). **Studies in Malaria with Special Reference to Treatment. Part VI. The Treatment of Benign Tertian Malaria with Peracrina 303.**—*Indian Jl. Med. Res.* 1927. Oct. Vol. 15. No. 2. pp. 277–286. With 2 charts. [6 refs.]

Peracrina 303 in doses up to 12 pills daily has been used for 10 patients in accordance with the makers' instructions—until no parasites had been found in the blood for 15 days. In six cases this result was reached in from 37 to 93 (average 72) days with two relapses while under observation for 8 weeks. The 4 remaining cases were treated from 72 to 112 (average 87) days when the supply of the drug gave out, but in none of them had the blood been free from parasites for 15 days. Patients objected to swallowing 12 large pills daily for two or three months, there was complaint of listlessness and loss of appetite, and depression due to the uncertain length of the treatment.

C. L.

SINTON (J. A.). **Studies in Malaria with Special Reference to Treatment. Part VII. The Intravenous Injection of Sodium Stovarsol in the Treatment of Benign Tertian Malaria.**—*Indian Jl. Med. Res.* 1927. Oct. Vol. 15. No. 2. pp. 287–299. [15 refs.] [Malaria Treatment Centre, Kasauli, India.]

These experiments were carried out at Kasauli, at an altitude which experience has shown to preclude reinfection, upon British soldiers 20 to 30 years of age, who had *P. vivax* detected in the blood immediately before beginning treatment and who had previously relapsed with that infection on an average four times. They were divided into experimental and control groups, being placed in one or the other in strict rotation, there being evidently 25 in the stovarsol group. The controls

obtained cinchona alkaloid in one form or another, either as quinine, cinchonine, cinchonidine or "malarene" which last "is a standardized 'cinchona febrifuge' prepared by the Director of Agriculture (Cinchona) Madras." It is clear then that a beginning has been made in putting out a standardized cinchona febrifuge in India. The total amount of alkaloid taken in each of the 4 treatments was 77 gm. (1,190 gr.), 36·5 gm. (560 gr.), 36·5 gm. and 36·5 gm., and the number of patients in each of the 4 control groups was 26 to 28. Sodium stovarsol patients fall into 3 groups: 1 who developed jaundice after the first injection, no more being given; 10 who received 1 gm. on the first and third days; and 14 who received 1 gm. on the first and 1·5 on the third and fifth days. Relapses with parasites in the blood within 8 weeks of ceasing treatment were in the 4 control groups 75, 74·1, 81·5 and 61·5 respectively; in the two sodium stovarsol groups 100 and 86·7 per cent.

After the stovarsol, all parasites disappeared in 5 to 30 (average 19·8) hours. In the case receiving 1 injection only, parasites reappeared in 7½ hours; among the 10 receiving two, in 12 to 37 (average 20·3) days; in the 14 receiving 3 injections, there was no reappearance within 8 to 9 weeks in 2, while, among the other 12, parasites were detected (in thick film as always) in 10 to 59 (average 23·9) days.

"We followed the course of the destruction of the parasites by hourly thin films in a number of cases. Our experiments bear out Marchoux's contention that this drug has a marked action on the larger pigmented parasites in the peripheral blood. This was especially seen in one case where gametocytes, mostly female, were present in every other field of the thin film before injection and could only be found with very great difficulty at the fourth hour after injection, although ring-forms of the parasite were still present.

"The effect on the smaller forms was very curious. The first effect noted, about an hour after injection, was an increase in size of the vacuole, a thinning of the protoplasm and a deeper staining chromatin dot. At the 4th to 6th hour the protoplasm of the ring-forms had become very thinned and in many cases was broken up into fine connected strands, sometimes with a ragged, cobweb-like appearance. The vacuole, if present, was very large and the chromatin seemed to be more deeply stained than normal. Another curious finding at this period was a large number of accolé forms, and many times double and treble infections of single cells were observed, although this had not been found before injection. Many of these forms and of the surviving larger forms seemed to be distinctly extracellular in position.

"The young unpigmented forms could be found for several hours after the larger forms were no longer detectable, but they were much diminished in number. The action of the drug seemed to prevent the normal increase in size of these young forms, or else destroyed them when they got to a certain stage, so that only small forms could be found. At this period the protoplasm stained very faintly and was irregular in shape and small in amount. The chromatin retained its staining power much longer.

"The impression which we got from a study of our preparations was that the parasite was being dissolved off the surface of the cell, rather than inside the cell as stated by Marchoux (1925)."

Stovarsol produced less splenic shrinking than quinine, and is apt, perhaps by the massive destruction of parasites, to induce high fever at its first injection. This setting free of a large quantity of malarial antigen prompts the suggestion that on YORKE and MACFIE's hypothesis the immunity reaction should be greater. It is suggested that it will perhaps be found greater in fresh infections. No toxic symptoms, except the one case of jaundice, were noted.

C. L.

WALKER (H. M.). **Mercurochrome 220 Soluble in the Treatment of Malaria.**—*Fifteenth Ann. Rep. Med. Dept. United Fruit Company, Boston, Mass.* 1926. pp. 60–62. [3 refs.]

The adult dose of mercurochrome was 15 cc. In two of nine cases tertian parasites disappeared. In the others a second dose was necessary—of the same size except in two in whom the first had produced marked stomatitis. In one of these seven, tertian parasites disappeared after the second dose; in three more the second dose was followed by no change in the tertian parasites present which persisted until quinine was given; in two tertian parasites disappeared but subtertian ones persisted until quinine was given. In the last quartan parasites were present and were unaffected by mercurochrome. "No cases were taken as controls, but we have kept in mind the fact, as proven in Ancon Hospital several years ago [and in the Medical College Hospital, Calcutta, at least 25 years ago], that rest in bed and an adequate diet will often result in a clinical cure with negative blood in cases of malaria, especially the tertian type."

C. L.

SPERANZA (U.). Il bismuto nella terapia della malaria. [**Bismuth in the Treatment of Malaria.**]—*Riv. di Malariologia.* 1927. May–June. Vol. 6. No. 3. pp. 573–578. [14 refs.] [English summary p. 708]. ["S. Spirito" Hosp., Rome.]

The English summary notes that bismuth, used as salbiolo in 12 severe malaria cases, is efficacious but inferior to quinine. Its use may be advantageous where quinine is not tolerated. Reference to the original shows that all but one of the cases were of subtertian malaria.

C. L.

ROSS (G. R.). **Alternative Treatment of Malignant Tertian Malaria in Quinine Susceptible Patients.**—*Jl. Trop. Med. & Hyg.* 1927. Oct. 15. Vol. 30. No. 20. pp. 257–263. [10 refs.]

Quinine, the most satisfactory anti-malarial drug, is contra-indicated in two conditions: (1) Where an idiosyncrasy to the drug exists—where, that is, there are only two factors at work, the drug and the tissue reaction to it; our dependence on quinine is such that unless there are major symptoms of intolerance quinine should be given. (2) When quinine has precipitated haemoglobinuria—where a third factor, the subtertian malaria parasite, has invariably been present. Here quinine administration during the acute attack must always be dangerous and alternative treatment is most desirable.

Regarding arsenic Ross's experience is illustrated by a case, 3 times a sufferer from blackwater fever always following quinine, treated unsuccessfully with methylarsenate of soda and novarsenobillion for a week. Haemoglobinuria immediately followed the administration of 5 grs. of quinine. Regarding mercurochrome, Ross notes that those who have used it have produced severe toxic symptoms and holds that their almost uniform unsuccess may reasonably be held to show that it has no direct ill effect on plasmodia, but that this does not exclude an effect in aiding tissue resistance which might show itself in small doses. He believes on evidence given that two or three injections of about 5 cc. of a 1 per cent. solution given during the first five days of an attack may produce an apyrexial interval with freedom from parasites

which will render quinine less likely to produce haemoglobinuria if it then be started.

Plasmochin too has been reported upon in 6 cases in which blackwater fever had previously followed quinine administration given for subtertian malaria, and in which the new drug was now administered in doses of 0·02 gm. 3 to 5 times daily. The conclusion is that while, like mercurochrome, it can effect a temporary cure, relapse almost invariably occurs. Quinine will then have to be given, the previous administration of plasmochin not having reduced nor increased the liability to haemoglobinuria. As to its effects on gametes, Ross is noncommittal, and he holds that, since confinement to bed has not in similar cases influenced these acute infections, the improvements [for instance in parasite findings] are to be attributed to the drug.

C. L.

SIMON (Italo). Della cura della malaria e di alcuni nuovi tentativi in proposito. [**Treatment of Malaria. Some New Drugs.**]—*Boll. Soc. Med.-Chirurg. Pavia.* 1926. Vol. 1. (New Series). No. 6. pp. 1161–1168. [2 refs.]

On the ground that quinine has not subdued malaria—because it has not been administered with the detailed considerations held necessary, because alimentary administration is not always tolerated, because the well-known state tablets of Italy may be passed intact in the faeces, because intramuscular injection is held to necessitate administration at a particular time of day which varies from case to case, because districts are too large for the medical men in them to cover properly, because the sick give up treatment too soon, and because a certain number of sick have, it is held, an idiosyncrasy for quinine—Simon considers the range of possible alternative remedies. In the first rank he places, in this order, quinine, cinchonine, "fenocolla" as indicated by the schools of ALBERTONI and CERVELLO, methylene blue, arsenical preparations, berberine, and certain Sardinian herbs quoted as *Ayuga iva* and *Erithraea centhaurium*. There follow three other groups—the first contains quinine with certain adjuvants, the second quinine with extracts of such organs as the spleen and adrenals, and the third certain remedies whose antimalarial properties are described as clear to those who prepare them but undiscoverable by pharmacologists and therapists. The last list contains smalarina, the only one of the group which has obtained fame outside Italy; and is doubtless capable of immense extension in other malarious countries. [There are not then included the three non-cinchona drugs which are at present most before the public as antimalarial remedies, mercurochrome, stovarsol and plasmochin].

C. L.

VOROBIEW. La méthode d'Appel dans le traitement du paludisme. [**Appel's Method for the Treatment of Malaria.**]—*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 7. French summary p. 470. [In Russian pp. 406–414.]

Vorobiew has treated 78 malaria cases by APPEL's method* and observed them for 7 months; only 19 per cent. have relapsed. In most

* APPEL's method (1918) consists in the administration of 0·2 gm. methylene blue solution intravenously, followed 4 hours later by neosalvarsan. For details see this *Bulletin*. Vol. 11. p. 29.—[Ed.]

cases the treatment has been repeated, and in 3·5 per cent. given 3 times. With this treatment gametes disappear much more rapidly than with any other.

C. L.

LEGENDRE (F. M. A.) & CIENFUEGOS (J. M. Alvarez). Sur quelques essais de traitements nouveaux du paludisme. [**New Forms of Treatment of Malaria.**]—*Bull. Soc. Path. Exot.* 1927. June 8. Vol. 20. No. 6. pp. 456–459. [2 refs.]

These tests were carried out on general paralytics after therapeutic inoculation of malaria.

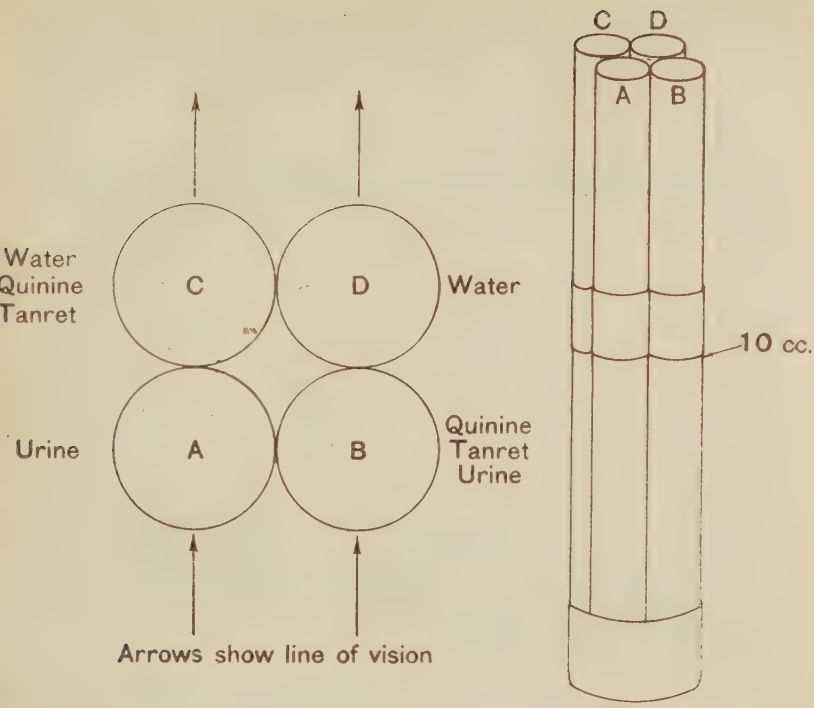
Stovarsolate of quinine 1 *gm. daily.* In one case of *P. vivax* infection parasites had disappeared by the third day. Treatment was continued for 5 days. There was no relapse. *P. malariae* was used in 4 cases. In one the drug was given for 8 days, the blood remaining negative over an observation period of two months; in a second for 7 days with blood parasite-free for 3 months. In the other two, infections had been induced 6 and 13 months earlier, and parasites had persisted since. Whether they were treated or not during this period is unstated. Stovarsolate of quinine caused in the one disappearance of schizonts in 2 days and of gametes in 7. In the other, who was afebrile, schizonts disappeared in 3 days and gametes in 11, the dose for the last 3 days being 1·5 gm. It is noted incidentally that in these *P. malariae* cases the spleen did not become palpable, and suggested that when this does occur there is an undetected associated tertian infection.

Nine different hydrochlorides of amino-alcohols from the Fourneau laboratory were tested without success.

C. L.

ROBINEAU (M.). Comparateur à quatre tubes pour le dosage de la quinine dans les urines, à l'aide du réactif de Tanret et d'une solution titrée de quinine. [**Determination of Quinine Content of Urine by using Four Tubes with Tanret's Reaction and a Standardized Solution of Quinine.**]—*Bull. Soc. Path. Exot.* 1927. July 13. Vol. 20. No. 7. pp. 591–595. With 2 text figs.

Robineau has described (this *Bulletin*, Vol. 23, p. 552) an apparatus by which with the aid of 30 tubes the Tanret reaction may be used to estimate the amount of quinine in the urine. A much simplified and apparently practical apparatus consists of 4 tubes clamped together and viewed in pairs, each pair containing the same constituents, the familiar arrangement used for determining the pH of liquids. The lower limit of the upper clamp marks a capacity of 10 cc. This quantity of quinine-containing urine is poured into A and B, the same quantity of water into C and D. To B and to C are added 20 drops of Tanret's solution. This solution must be in excess, and it is found that with this quantity this is the case. If there is quinine in B an opacity will be produced whose density will vary with the quantity of quinine. A one-in-five-thousand solution of quinine (estimated as base) is dropped into C, drop by drop, until an equal opacity is observed in the two pairs of tubes, the amount of quinine involved being read off from a



Simplified apparatus for determination of Quinine Content of Urine by the Tanret reaction method.

table. [The two pairs of tubes are evidently strictly comparable, but there must be standardization of the drop—a pipette of fixed nozzle size and a drop not oftener than once a second—before the figures in the table can be always accurate.]

C. L.

SCHACHSUWARLY (M.). Das Verhalten des Serumbilirubins bei Malaria. [**Behaviour of Bilirubinaemia in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Sept. Vol. 31. No. 9. pp. 399–413. [54 refs.] [Inst. for Ship & Trop. Diseases, Hamburg.]

The author's considerable investigations include 13 cases of tertian and 27 of subtertian malaria, 6 normal persons, and a number with various complaints. It is concluded that bilirubinaemia is increased as the result of the malarial attack, disappearing some days after it ceases; but that with latent malaria, even if parasites are present in the peripheral blood, the blood content is normal for bilirubin. Its absence, then, does not exclude latent malaria.

C. L.

MORISHITA (Kaoru), FURUTAMA (Taro) & NAMIKAWA (Hiroshi). **On the Behaviour of Urobilinogen in Chronic Malaria, with an Account of its Diagnostic Value in Malaria Prevention Work.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1927. Sept. No. 270. English summary pp. 9–11. [In Japanese.] [Govt. Research Inst., Formosa, Japan.]

In connexion with an attempt to establish a relationship between malarial infection and urobilinogen, the writers have examined 2,684 Japanese, Formosan Chinese, and savages. The result is tabulated thus:

Strength of reaction.	Parasite rate.	Spleen rate.	Combined parasite and spleen rate.
+++	28·8	75·8	79·1
++	18·7	60·1	60·1
+	14·1	33·4	57·1
±	10·4	45·6	50
—	5·3	23·1	30·4

Moreover, the urobilinogen markedly decreased in a certain locality after two months quininization of the entire community. It is concluded that urobilinogen in the tropics is mostly due to malaria, and that those showing this condition, but no parasites, should be suspected and kept under observation.

C. L.

MORISHITA (Kaoru) & FURUTAMA (Taro). **Some Observations on the Adrenalin-Reaction in Latent Chronic Malaria.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1927. June. No. 267. English summary pp. 1–2. [In Japanese.] [Govt. Research Inst., Formosa.]

The investigation reported was carried out on 30 persons who showed enlarged spleen and urobilinuria, but no clinical evidence of malaria and no parasites in the blood. The adult dose of the 1 in 1,000 solution used was 0·75 cc. and the blood was then examined by thick film at intervals up to 48 hours. Parasites appeared in 3 cases (at 0·3, 1 and 2 hours respectively) in small numbers and without a febrile attack. In 15 of the negative cases further examinations up to 1 or 2 months showed the appearance of parasites in 3 cases. The number of parasites in the peripheral blood reached its maximum 5 to 90 minutes after the splenic contraction. It is suggested that the increase is the result partly of a mechanical expulsion of parasites, partly possibly biological since "the adrenalin hyperglycaemia may provide especially favourable conditions for the blood protozoa."

C. L.

NEPRJACHIN (G. G.). Zur pathologischen Anatomie des Gehirns bei Tropenmalaria. [**Morbid Anatomy of the Brain in Tropical Malaria.**]—*Frankfurter Ztschr. f. Path.* 1927. Vol. 35. No. 1. pp. 143–150. [19 refs.] [Path. Anat. Inst., Univ. Kasan.]

Neprjachin has examined the brains of 18 persons dead of malaria. The findings are practically those already fully recognized, but do not

include the " malaria granuloma " of DÜRCK and other writers, which accordingly cannot be considered as specific for malaria [see this *Bulletin*, Vol. 23, p. 626].

C. L.

WARASI (W.). Das Knochenmark dei der Malaria tropica. [**The Bone Marrow in Subtertian Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Sept. Vol. 31. No. 9. pp. 435–436. [Trop. Dis. Inst., Tiflis.]

In ten cases the red marrow from the ribs was examined as smears with these findings : Myeloblasts were vacuoled in nucleus and protoplasm. Myelocytes were unaltered, but very few were eosinophil. Some macrophages took the stain poorly, others showed an intense phagocytosis of parasites, pigments and damaged erythrocytes. All megakaryocytes showed diminished protoplasm and polymorph nuclei staining poorly except for a contrary condition at their margins. The usual active karyokinesis was lessened. In 3 cases the proportion of non-infected to infected corpuscles was noted : it was as follows :—

Peripheral blood ...	6 to 1		
Brachial artery ...	59 to 1		
Vena porta	16 to 1		
Splenic pulp	7·5 to 1	48 to 1	36 to 1
Red marrow	23 to 1	105 to 1	61 to 1

In the bone marrow the whole schizogonic cycle can be observed. There has been seen once " parthenogenesis " of gametes, and once a grown pigmentless schizont.

C. L.

MASSA (Mario). La glicemia nella malaria. [**Glycaemia in Malaria.**]—*Pathologica.* 1927. Nov. 15. Vol. 19. No. 433. pp. 535–541. [23 refs.] [Inst. Path. & Clin. Med., Univ. Sassari.]

The writer tabulates the sugar findings in the blood in 28 malaria cases. Where fever was absent the blood sugar content was about normal. In new infections, and in relapses following a long apyretic interval, it is especially noteworthy that the sugar rises rapidly during the rigor, becoming about normal at the height of fever, and subnormal at the beginning of apyrexia. If relapses are numerous and close together the alteration in the blood sugar is insignificant.

C. L.

VAN NITSEN (R.). Réveil de la malaria par les injections de gonacrine. [**Awakening of Malaria by Gonacrine Injections.**]—*Bull. Méd. du Katanga.* 1927. Aug. Vol. 4. No. 2. pp. 47–48.

Gonacrine has been employed with varying success in the treatment of gonorrhoea in injections of 5 cc. of a 2 per cent. solution. van Nitsen describes 4 cases in which, not necessarily after the first injection, there resulted acute accesses of malaria with schizonts in the blood, which in one case was not warded off by preliminary administration of 1·5 gm. of quinine. The drug appears, then, to have a provocative value.

C. L.

MANSON-BAHR (Philip). **Researches upon the Production of Malaria Antigen for a Complement-Deviation Test.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1927. July 11. Vol. 21. No. 1. pp. 63–68. [9 refs.]

Manson-Bahr briefly reviews the efforts of THOMSON and THOMSON [this *Bulletin,* Vol. 2, p. 554; Vol. 13, p. 87] to obtain a malaria antigen by extracting cultures of malaria parasites with that excellent protoplasmic solvent, decinormal caustic soda. He attributes his own failure to obtain a satisfactory antigen by similar means to the quantities of extraneous proteids which such a solution must necessarily contain. Having in mind FAIRLEY'S work on schistosomiasis, in which this worker obtained a specific antigen from the larval stages during their non-sexual multiplication in the molluscan host, he attempted to obtain a specific malarial antigen from those multiplicatory oöcystic stages in the anopheles which follow the sexual act. Although supplied with large numbers of *A. maculipennis* by Colonel S. P. JAMES of the Ministry of Health, great difficulty was experienced in rearing from these numbers sufficiently great for insects to be always available to feed on any tertian case with sufficient gametocytes when it should at any time present itself. The development of *P. falciparum* was found to be less certain and satisfactory than that of *P. vivax* in like conditions. The best foods for the larvae were the alga *Enteromorpha intestinalis* and "Piscidin," a proprietary substance obtained from Hamburg. Nevertheless in spite of specially constructed incubators, two years' work resulted in only 26 stomachs infected with *P. vivax.*

Accordingly, attention was turned to the allied bird malaria. Two infected canaries were received from Edmond SERGENT of Algiers, but it did not prove possible to infect from these, sparrows, *Culex fatigans* or other canaries. 100 sparrows were next shipped from Bombay; 60 arrived in England, the others having apparently died of overwhelming infections. Of the survivors, 12 were sufficiently heavily infected on arrival to infect culex, although parasites had entirely disappeared a month later. Canaries inoculated from these 12 became either so heavily infected as to die or so lightly infected as to be useless for mosquito experiments, while in infected mosquitoes the number of oöcysts did not approach those produced by *P. vivax.* The antigens used were alcoholic extracts, 1 in 10, of the 26 anopheles and 24 culex stomachs which contained oöcysts. They were free from anticomplementary and haemolytic properties, but no fixation of complement occurred.

The experiments have been published in the hope that further efforts on these lines will be made where malaria and anopheles are abundant. The conditions necessary for the success, which it is believed will be achieved, are held to be the extraction of at least 100 heavily infected stomachs to every 1 cc. of absolute alcohol, preservation for a short time only, and evaporation with extraction of the residue in normal saline before use.

C. L.

HENRY (X.). [Contribution à l'étude sérologique de l'infection palustre.] [**Serological Study of Malaria.**]—*51e Congrès de l'ass. franc. pour l'avanc. des Sc., in Gaz. hebd. Sc. méd. Bordeaux.* 1927. Vol. 48. p. 311. [Summarized in *Bull. Inst. Pasteur.* 1927. Aug. 31. Vol. 25. No. 16. p. 702.]

It appears from the abstract that 1 cc. of a 1 per cent. solution of methylarsenate of iron is added to 0·1 cc. of unheated human serum,

the mixture is shaken and incubated for 1½ hours at 37° C., removed from the incubator and examined half an hour later. In malarial serum [as the abstract notes, the species of plasmodium is not mentioned] there occurs flocculation. The investigation was carried out on 58 malaria cases and 85 healthy persons.

C. L.

TALIAFERRO (William H.), TALIAFERRO (Lucy Graves) & FISHER (Anna B.). **A Precipitin Test in Malaria.**—*Fifteenth Ann. Rep. Med. Dept. United Fruit Company, Boston, Mass.* 1926. pp. 48–57. [12 refs.]; also in *Jl. Preventive Med.* Baltimore. 1927. May. Vol. 1. No. 5. pp. 343–357. [11 refs.] [Univ. Chicago.]

The best antigen was obtained from malarial placenta, the pulpy part minced by machine, an equal quantity of ether added, the mixture stood for 18 days, the ether rejected, and the *insoluble* residue extracted with Coca's solution, which is water containing the following percentages of salts—sodium chloride 0·5, sodium bicarbonate 0·05, carbolic acid 0·4. This preliminary extraction with ether seemed to increase the potency of the antigen, which was obtained as a clear fluid by filtering the extract in Coca's solution through hard filter paper (Whatman's No. 5). A table is given showing that of 54 persons found infected, all but 11 by thick film, 83 per cent. were unquestionably positive, while of 32 persons in whom infection was not discovered, although a thick film was used in 4 only, 78 per cent. were unquestionably negative, and it would be surprising were not some of these, in whom no parasites were thus detected, really infective. In 6 of those positive to a presumably pure subtertian antigen, only tertian infection was discovered, and in 4 of them the reaction was very marked. The test was carried out thus—The tubes had a length of 50 mm. and a bore of 4 mm. The solution of antigen and of undiluted patient's serum were used, each to the extent of 0·15 cc. that which was the heavier, generally the serum, being placed by pipette at the bottom of the tube, and the lighter one carefully placed above it without mixing. They are incubated at 37° C. for an hour, and then placed in the ice box for 6 to 9 hours. A ring of precipitate appears at the junction of the two fluids in positive cases. "Some results indicate that efficient antigens can be prepared from infected red blood cells, provided they have a preliminary extraction with ether. All of the data indicate that the precipitation is a specific antigen-antibody reaction, and not a non-specific flocculation."

C. L.

STEPHENS (J. W. W.) & OWEN (D. Uvedale). *Plasmodium ovale.*—*Ann. Trop. Med. & Parasit.* 1927. July 22. Vol. 21. No. 2. pp. 293–302. With 28 figs. on 2 plates (1 coloured). [12 refs.]

Another case of *P. ovale* is reported, this time from Nigeria, the coloured plates which accompanied the original report of the case from East Africa being reproduced. The red cell is often regularly or irregularly oval, often with decolourization, and with stippling less marked than with *P. vivax*. The parasites are not amoeboid but round or oval, with coarse dark abundant, often yellowish brown pigment; spores are large, with 14 as a maximum number. When they are 8 or 10 they form a regular daisy with central pigment and completely fill the red cell, strikingly resembling quartan. Equatorial forms and

multiple infections are rare. Gametocytes resemble those of quartan malaria in a stippled cell with decolourized margin. The periodicity remains undetermined. The writers are unable to identify *P. ovale* with *P. vivax minutum* Emin.

C. L.

PAWAN (J. L.). **The Relative Number of Male and Female Crescents in the Peripheral Blood.**—*Ann. Trop. Med. & Parasit.* 1927. July 22. Vol. 21. No. 2. pp. 135–136. [1 ref.]

Among 3,304 crescents examined during five consecutive days the percentage of females varied from 68 to 80 with an average of 75. The sex of 3·5 per cent. could not be determined.

C. L.

PEWNY (Walther). Ueber Malariakulturen. [**Cultivation of Malaria Parasites.**]—*Wien. Klin. Woch.* 1927. Oct. 27. Vol. 40. No. 43. p. 1358.

It appears that HORNS and KAUDERS, at a meeting of the Association of Medical Men in Vienna [Gesellschaft der Arzte], stated that in culture the tertian parasite tended to form gametocytes. Pewny writes that during the war he worked in Albania in No. 58 Field Laboratory on this point. He modified Bass's medium and used 1 cc. of dextrose broth, 0·2 cc. of inactivated serum and 1 cc. of infected red corpuscles, cultured at 37° C. and found that subtertian rings developed to crescents, the beginning of crescent formation being already evident in the fifth hour. Development was hastened by addition of 0·1 cc. of a 3 per cent. solution of hydrogen peroxide, while the addition of glycerine was harmful. Living forms were still evident on the 17th day. Gametocytes are then formed in culture both by tertian and subtertian parasites. [SINTON (this *Bulletin*, Vol. 23, p. 814) reported crescents alone as being present in a culture overlooked for 10 days.]

C. L.

WAGNER-JAUREGG (Julius). Die Impfmalaria an der Wiener psychiatrischen Klinik. [**Inoculation Malaria at Vienna.**]—*Wien. Klin. Woch.* 1927. Sept. 8. Vol. 40. No. 36. pp. 1121–1122.

The originator of the malaria treatment for general paralysis sums up part of his experience. This treatment is withheld only in cases of galloping paralysis. Mortality has almost ceased ; the proper dosage, that is, has been determined. Attacks are usually limited to 8, rarely exceed 10. Cardiac tonics and nervous sedatives are administered. If there is danger, a small dose of quinine is given and, if that does not lessen fever, this is broken off by a full quinine treatment ; and an injection of malaria is repeated a few weeks later. Indeed in grave cases only 2 or 4 malarial attacks are allowed before giving quinine, neosalvarsan follows for some weeks, malaria is reinjected and allowed to run to 4 to 6 further attacks. If the first malarial course has not effected full benefit, a second is given with full and lasting advantage. There is at first no parallelism between changes in the serum and cerebrospinal fluid and the clinical improvement, but in cases which remain free from mental relapse these findings have become normal in 2 or 3 years. It is, however, advised that if a lumbar puncture does not show

normal conditions within a year at most, a second malarial injection should be given. As a rule this renders the fluid normal. Neosalvarsan to the extent of 3·15 to 4·95 gm. should follow every malarial treatment. The malaria has, in 2,000 cases, invariably been cured by 5 gm. of quinine given within one week and it is given whether malaria has aborted or not.

C. L.

PLEHN (A.). Die Behandlung der progressiven Paralyse mit Malaria tropica. [**Treatment of G.P. with Subtertian Malaria.**]—*Med. Klin.* 1927. July 15. Vol. 23. No. 28 (1179). pp. 1061–1062.

Plehn's reasoned standpoint is as follows. It is not to be expected that a second tertian malarial infection will benefit a general paralytic. Something else must be found or he must be left to his fate. Since an attack of tertian does not protect from one of subtertian malaria, the latter should at least be borne in mind in this respect ; and it is believed that with certain precautions it may be used with a safety which in the circumstances is reasonably sufficient, for he has employed it in 50 cases with one death. In Germany the danger of subtertian malaria seems to lie essentially in the primary attack. This must be closely watched with blood examination at least once daily. If this examination shows 10 per cent. of the red corpuscles infected a second is made 8 to 10 hours later, and if the percentage has not lessened, quinine is given. The giving of half a gram of quinine may have no effect. It may on the other hand cause disappearance of the parasites. In the latter case there has followed, in Germany, a relapse in about 18 days, reasonably controllable and it has been the case that the febrile attacks have been stronger than with the tertian parasite. Moreover a second infection with subtertian malaria has the less violent characters associated with relapses of the primary one. It is, then, concluded that when tertian malaria fails it is justifiable to use the subtertian form.

C. L.

KIRSCHBAUM (W.). Weitere Beobachtungen zur Klinik und Parasitologie künstlicher Malariainfektionen. [**Symptoms and Parasitology in Artificial Malaria Infection.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Aug. Vol. 31. No. 8. pp. 349–365. With 4 figs. in text. [12 refs.] [State Hosp., Friedrichsberg-Hamburg.]

This useful summary and confirmation of the work of others brings out the following points. The incubation of quartan malaria (after injection of infective blood) is longer than of tertian, namely 4 to 10 days after intravenous and 21 days after subcutaneous injection, and after a second or third infection the incubation period is longer than after a first. Spontaneous disappearance of tertian malaria occurs in 10 per cent. of first infections and 77·3 per cent. of reinfections, a condition held to be exceeded in natural infections. That spontaneous disappearance does not imply complete immunity is shown by the not infrequent appearance of relapse. Tertian injected malaria has, generally, in first infections a prodromal fever, in reinfections generally none, this being absent in quartan infections also. After a second or third infection a resistance to tertian infection appears, which, according to JAMES and SHUTE, does not withstand a mosquito infection. Natural resistance to injected malaria is not established for Germans. Strains

of tertian malaria of varying origins have the same clinical effects, although the individual reactions may greatly vary, and a resistance acquired to one strain holds against others. The differences which quinine shows in different individuals are an indication of differing resistance to the tertian parasite. Prophylactic doses of quinine given before injection are useless; and a case is cited where daily "subcutaneous" injections of 0·3 gm. [5 gr.] of quinine were given for 40 days after subcutaneous injection of 4 cc. of tertian infected blood with the outbreak of frank tertian malaria 14 days after the cessation of this treatment. Quinine hydrochloride in dosage of 0·25 gm. may inhibit the fever for a time.

C. L.

KAUDERS (O.). Immunitätsstudien bei Impfmalaria. [**Immunity Studies in Inoculation Malaria.**]—*Cent. f. Bakt.* I. Abt. Orig. 1927. Vol. 104. No. 1-4. pp. 158–160.

It is established that to induce a second malarial infection repeated injections may be required. If it is effected, the incubation period is prolonged, the infection tends to die out after 4 or 5 attacks, and it may or may not be provocable. Is this the result of immunity? Kauders has given to 12 cases of malaria either 1 or 2 injections of 1 to 2 cc. of the serum of a patient in which infection has died out—refractory serum. In three there was no effect, in nine there was. In five the fever disappeared and could not be provoked nor did it spontaneously return. Serum from normal persons, or from those actually suffering from a malarial attack, was without result. On the other hand a series of 7 to 9 similar injections given to a person before malarial blood was injected did not prevent infection. Indeed the incubation period was strikingly shortened. In a third series, malarial blood was injected and also some 8 injections of refractory serum given—one such case has had 12 subsequent malarial injections and a number of provocative injections, but has had no malaria within the 5 months' observation period. Three cases ran a normal course, in two the malarial attacks numbered 4 and 5 and then disappeared; and a second injected infection behaved similarly.

Kauders has also investigated malarial blood cultures using half per cent. sodium citrate solution, defibrinated blood and blood agar, blood mixed with gelatin as 1 to 5, clotted blood, defibrinated blood and examined them every 12 hours. In all 5 conditions parasites became extra globular after 12 hours and extraordinarily like gametes. In some cases gametes are identifiable, and after 88 hours only gamete-like forms are to be found, although in degenerate state. It is pointed out that a pure culture of gametes would settle the question of "parthenogenesis."

C. L.

WILLIAMS (R. G.). **The Functions of the Liver as affected by Malaria induced in General Paralytics.**—*Lancet.* 1927. Nov. 19. pp. 1071–1073. With 4 text figs.

Laevulose tolerance curves were carried out on 16 general paralytics and one tabetic under tertian malaria treatment, on 4 cases of gross liver disease (two of cirrhosis confirmed at autopsy, one of acute yellow atrophy and one of secondary malignant growths) and 6 general

paralytics untreated by malaria. The van den Bergh test seemed less sensitive than that of laevulose tolerance. The liver function was found to be much more severely affected in malaria than in the other conditions investigated, and it is concluded that the laevulose tolerance test, carried out in series, satisfactorily estimates liver derangement, and is useful in controlling therapeutic malaria.

C. L.

WETHMAR (Rudolf). Blutgruppen und Impf-Malaria. [**Blood Grouping and Inoculation Malaria.**]—*Klin. Woch.* 1927. Oct. 8. Vol. 6. No. 41. pp. 1947–1948. [4 refs.] [Wittenauer Sanatorium & "Robert Koch" Inst., Berlin.]

In the matter of connexion between blood groups and the transmission of injected malaria, which has been attracting attention in Austria, Wethmar has determined the grouping of donor and recipient in 65 cases. With intravenous injection in cases where the two fell in favourable, or compatible, groups there was an average incubation period of 4·5 days, the type of fever was double in 46 per cent., single in 27 per cent. and mixed in 27 per cent.; while with unfavourable groups the figures were 8·2 days, 6 per cent., 82 per cent. and 12 per cent. With intracutaneous injection and favourable grouping the incubation period was 9·8 days, and the type of fever was double, single and mixed in 13, 67 and 20 per cent.; while with unfavourable grouping the figures were 15·1, 8, 92 and 0 per cent. Moreover the incubation period of those with favourable groups took an uneventful course while that of those falling in unfavourable groups was sometimes (9 of 28 cases) marked by occasional shivering and a rise of temperature.

C. L.

RUBASCHKIN (W.), MOLDAWSKAJA (W.) & PAULI (S.). Blutgruppen und Malaria. [**Blood Groups and Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. July. Vol. 31. No. 7. pp. 329–339. [1 ref.] [Ukraine Protoz. Inst. Kharkov.]

The writers' conclusions are that the agglutination of red corpuscles is increased in malaria particularly during fever and falls with the temperature curve. The rise in the agglutination curve during incubation foreshadows an acute attack. Variation in the possibility of agglutination of red cells of group AB. (IV) affects only one of the two agglutinogens.

C. L.

STUART (M. A.). **Measures of Outstanding Importance in the Prevention and Control of Malaria.**—*U.S. Nav. Med. Bull.* 1927. Oct. Vol. 25. No. 4. pp. 996–1010. [9 refs.]

This is a résumé for the benefit of U.S. Naval Medical Officers of recent work on malaria familiar to readers of this *Bulletin*. One paragraph deals with work of DARLING which is perhaps not widely known.

"In general, the effect of an irritating, toxic, or otherwise unusual fluid on mosquito larvae is to hasten pupation. A number of experiments were tried with sea water, salt water, and solutions of the heavy metals, and in most instances, in the more concentrated solutions, when the larvae were not killed within 24 hours, they pupated, and occasionally the period of pupation was shortened; so that if, for instance, sea water were used

as a larvicide, the first effect would be to hasten pupation, and thus increase the number of anopheles in a district, and if later the sea water became diluted by rain, several species of malaria-transmitting anopheles might breed in it without difficulty, notably *A. albimanus* and *A. tarsimaculatus*. On this account sea water could not be used with any degree of success as a larvicide for anophelines, except in large quantities and in certain locations."

C. L.

CARDAMATIS (Jean P.). Compte rendu sur notre activité pendant la mission de l'été 1926 pour la restriction du paludisme en Thrace et Macedoine. [**The Mission of Summer, 1926, for the Restriction of Malaria in Thrace and Macedonia.**]—*Grèce Méd.* 1927. Mar.-Apr., May-June & July-Aug. Vol. 29. Nos. 3–4, 5–6 & 7–8. pp. 9–14 ; 23–24 ; 32.

The million refugees which have reached Greece since 1921 suffered pitiably from malaria up to 1925. They were mainly uninfected, mixed with a few from malarious districts and deposited largely in spots notoriously malarial. In certain localities a fifth of them died, for quinine was hopelessly inadequate in quantity. The winter 1924–25 was exceptionally cold and dry, the drought being continued into the summer of 1925, so that most hibernating mosquitoes were killed and the survivors prevented from breeding. In 1925 quinine became abundantly available and housing was becoming adequate. Moreover, the refugees pluckily set to work on intensive cultivation which transfigured the land, an item on which great stress is laid ; the State provided the means for them to obtain medical aid ; and further infected refugeees ceased to arrive. These factors could clearly never have operated had it not been for the arduous, complete, and personal propaganda tours, aided by the cinematograph, which the Inspector of Malaria undertook. As a result, it is noted, malaria in Thrace and Macedonia has not only lost its worst characters but has ceased to be a racial menace.

C. L.

CASTIGLIONI (Arturo). **Italy's Campaign against Malaria.**—*Brit. Med. Jl.* 1927. Aug. 13. pp. 278–279.

The paper is permeated by a sense of high and ancient heritage and modern national progress. Much that it contains is familiar to readers of this *Bulletin*. Sardinia, like its neighbour Corsica, presents the most pressing national malarial problem although parts of Sicily run it close. Malaria has been notified as an occupational complaint and the entire cost of protection of workers is thrown on landowners and contractors. It is definitely stated that in certain parts of Italy—the district of Schito between Castellamare di Stabia and Torre Annunziata is particularly mentioned—anopheles no longer bite man and malaria is disappearing ; and that in other places such as San Rossore, near Pisa, they bite only up to July, thus causing the malaria to take on a very mild character.

C. L.

MISSIROLI (A.). La prevenzione della malaria nel campo pratico. [**The Prevention of Malaria in Practice.**]—*Riv. di Malariologia.* 1927. May–June. Vol. 6. No. 3. pp. 501–572. With 21 figs. & 2 maps. [1 ref.]. [English summary pp. 707–708.] [Anti-Malaria Experim. Station, Rome.]

Certain experimental antimalarial measures were employed under the supervision of the Director General of Public Health and with the co-operation of the International Health Division of the Rockefeller Foundation, in Portotorres, Sardinia, and Bianconovo, Calabria, during 1925. In the following year operations were extended to cover a wider field.

The prevalence of malaria was gauged by the splenic, parasitic, and haemoglobin indices, the number of cases of malaria among children born during the year and among persons immigrating from districts known to be free of the disease, the total number of cases treated during the year, and the records of absences of children from schools.

As a larvicide commercial Schweinfurt green was used, containing some 56 per cent. of arsenious anhydride. Different samples vary in composition ; it is, therefore, necessary to analyse each before use. It is heavier than water, and sinks in 24–36 hours. The smallest amount found effective was 5 gm. per 100 sq. metres ; twice this strength was employed. As diluents ordinary street dust, slaked lime, ashes, and sand, gave equally good results ; the first was the cheapest. The mixture was distributed either by bellows worked by a man from a boat, or, if there was much reedy vegetation, by hand or from an aeroplane.

Treatment was by bisulphate or hydrochloride of quinine in tablets, tannate in chocolate-drops, or other salts in powder within gelatin capsules. The drug was given daily for 60 days ; 4 tablets night and morning for 6 days, 4 in the afternoon or evening for the next 15 days, and 3 daily for the last 40 days, for adults.

The results obtained are presented graphically. The daily capture of mosquitoes, for example, ranged between 50 and 400 in Portotorres, a small town of 6,000 inhabitants. Female mosquitoes far outnumbered males. The chief species was *A. maculipennis*. In Bianconovo, *A. maculipennis* and *A. superpictus* were transmitters ; in Brancaleone the latter predominated, particularly in June and July.

In Sermoneta 56 per cent. of 905 inhabitants took an average of 24·9 gm. of prophylactic quinine each. In Torpé only 19 per cent. took it. During the first year no noticeable reduction of the splenic index was seen ; during the second year it had fallen at Bianconovo from 56·2 to 29·2, and in Portotorres from 46·8 to 27. The fall in the parasitic index was very marked and progressive ; thus, it fell in Bianconovo from 17·8 in 1925, to 10·3 in 1926, and to 0·4 per cent. in 1927. In Portotorres for the same period, the figures were 34·2, 8·7, and 5·9 per cent.

The number of children born during the year who were attacked by malaria was 2·6 per cent. in 1925, nil in the following year ; in Portotorres, however, there was a slight increase. The number of cases treated in the year fell to zero in the second year at Bianconovo, and to 75 in Portotorres in August, the highest figures for the preceding years in this town being above 400 in 1924 and 250 in 1925.

The campaign has, therefore, been most successful in Bianconovo, whence malaria has been practically abolished, while the benefits at Portotorres are so marked that now only a few sporadic cases are seen.

The report shows abundantly the good which can be achieved by drainage, agriculture, the treatment of patients, and the use of larvicides and of quinine prophylactically.

H. Harold Scott.

ESCALAR (G.). L'opera del Governatorato di Roma contro la malaria infantile nell'Agro Romano. [**Measures taken by the Government of Rome against Malaria in Children.**]—*Policlinico.* Sez. Prat. 1927. Sept. 26. Vol. 34. No. 39. pp. 1402–1403.

In its anti-malaria campaign in the suburbs of Rome the Administration has directed particular attention to children up to 10 years of age, determining the condition of blood and spleen, the hygienic state of their homes and the schools they use. These children have constituted 30 per cent. of all suffering from fever, malaria being established by blood examination. In the spring of 1927 the blood of 783 healthy scholars was examined—with no parasites found—a condition attributed to the prophylactic measures employed. The splenic index was 21 in the spring of 1926 and 12 in that of 1927. Again, the incidence of fever in schools during October-November was 1·1 per cent. and apart from schools 10 per cent. The measures employed included capture of insects, repair of nets, prophylactic quinine and the issue of 500 nets to protect cradles. In the Ettore Marchiafava antimalarial sanitarium there are educated, cured and instructed 50 to 100 children at a time. They remain there about 2 months. Their total number for 1926 was 489, nearly all gamete carriers. A malaria film, showing the Administration's efforts to combat infantile malaria in the Agro Romano, is in use.

C. L.

PECORI (G.) & ESCALAR (G.). Relazione sulla campagna antimalarica del 1926. (**The Antimalarial Campaign of the "Governatorato" of Rome in 1926.**)—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 244–267. With 1 chart in text & 1 map. [English summary pp. 491–492.] [Health Office, "Governatorato" of Rome.]

Antimalarial measures of all kinds have been carried out at a cost of 3,000,000 liras in the Rome administration. There has occurred an increase in population and houses, a halved death-rate and fewer cases treated.

BARD (Leopoldo). **Malaria in the Argentine Republic. Preventive Measures.**—*Jl. Trop. Med. & Hyg.* 1927. Sept. 1. Vol. 30. No. 17. pp. 217–218.

It is suggested that the proposed sanitary tax for defence against malaria in those parts of the Argentine Republic where it is prevalent should be raised by imports on beer and, indeed, on any alcoholic beverage.

SCHWARTZMANN (A. I.). L'épidémie paludique à Kazan en 1925. [**The Malarial Epidemic at Kazan in 1925.**]—*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 7. French summary p. 469. [In Russian pp. 414–422.]

Malaria increased greatly in Kazan in 1925. This is attributed to the greater development of *P. falciparum*, excessive summer heat having favoured the increase both of anopheles and of this plasmodium.

DORÉ (G. R.). La réactivation endocrinienne du paludisme. [**Endocrine Reactivation of Malaria.**]—*Bull. Soc. Path. Exot.* 1927. Oct. 12. Vol. 20. No. 8. pp. 718–719.

The significance of this report is indicated by Marcel LEGER's comment upon it—that in a case of tuberculosis in which malaria parasites are not found a febrile attack following an intravenous injection (in this case of postpituitary extract) can be explained without calling in malaria.

GONZALEZ OLAECHEA (Max.). Sindrome cerebeloso de origen malárico. Comunicación enviada a la Academia Nacional de Medicina de México. [**Cerebellar Syndrome of Malarial Origin.**]—*Crónica Méd.* 1927. Apr. Vol. 44. No. 766. pp. 101–111. With 1 text fig.

A man with *P. falciparum* infection had a zigzag walk with loss of equilibrium. The symptoms and the nerve tracts are considered in great detail. After four months quinine treatment he completely recovered.

ABEN-ATHAR (Jayme). *Plasmodium vivax* e *Plasmodium falciparum.* (Considerações sobre a sua alternancia mensal). [*P. vivax* **and** *falciparum.* **Their Monthly Variations.**]—*Sciencia Med.* 1927. May 31. Vol. 5. No. 5. pp. 225–234. With 1 folding chart and 2 text figs.

The writer looks on *P. vivax* and *P. falciparum* as constituting two races. They conjugate together and will produce offspring on Mendelian lines according as to which is regressive or dominant. The monthly variations he couples with their combinations.

C. L.

ANDERSON (John). The Present Position of Malaria.—*Caduceus.* Hong Kong. 1927. July. Vol. 6. No. 2. pp. 105–115. [31 refs.]

ASCOLI (Vittorio). La missione della Scuola Superiore di Malariologia. Discorso per l'inaugurazione del 1 Corso.—*Policlinico.* Sez. Prat. 1927. July 11. Vol. 34. No. 28. pp. 991–994.

BARBER (M. A.) & COOGLE (C. P.). Malaria among Mexican Cotton Pickers imported into Mississippi.—*Public Health Rep.* 1927. May 20. Vol. 42. No. 20. pp. 1368–1370.

BATTAGLIA (Mario). Di alcune febbri malariche continue. Nota clinica.—*Riforma Med.* 1927. July 4. Vol. 43. No. 27. p. 635.

CLARK (Oscar). Impaludismo simulando nephrite com edemas (hydropisia palustre).—*Brasil-Medico.* 1927. July 16. Vol. 41. No. 29. pp. 717–719. With 1 text fig.

COMYN (Kenneth). Antimalaria Work at Moascar, Egypt, in 1925 and 1926, and the Results compared with the Previous Two Years.—*Jl. Roy. Army Med. Corps.* 1927. July. Vol. 49. No. 1. pp. 14–26. With 1 plan & 1 chart. [2 refs.]

FERRÁN (Jaime). Tentativas de inmunización contra el paludismo mediante una vacuna anti-anofélica.—*Riv. di Malariologia.* 1927. Mar.–Apr. Vol. 6. No. 2. pp. 410–413. [English summary p. 494.] [Ferrán Inst., Barcelona.]

GALLAIS (G.). Réveil du paludisme à la suite de brûlures chez un paludéen sans crise depuis 14 ans.—*Rev. Méd. et Hyg. Trop.* 1927. May–June. Vol. 19. No. 3. pp. 82–83.

GRAHAM (J. W.). A Case of Palsy of the Upper Extremity possibly due to Malaria.—*Kenya & East African Med. Jl.* 1927. Aug. Vol. 4. No. 5. pp. 148–152.

IRAMINA (K.). Epidemiologische und klinische Beobachtungen ueber Kindermalaria in Sudôst-Formosa.—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1927. Apr. No. 265. German summary p. 5. [In Japanese.]

KNOWLES (Robert) & SENIOR-WHITE (Ronald). Malaria. Its Investigation and Control with Special Reference to Indian Conditions.—pp.vi+220. With 42 figs. & 6 plates & 29 figs. in Appendices II and III. 1927. Calcutta: Thacker, Spink & Co. [Rs. 7–8.] [*v. Bull. of Hyg.* Vol. 2. p. 765.]

LANOUE (H.). Le traitement du paludisme.—*Bull. Soc. Méd. d'Haiti.* 1927. July. Vol. 1. No. 3. pp. 84–91.

MOUZON (J.). La plasmoquine.—*Presse Méd.* 1927. Oct. 26. Vol. 35. No. 86. pp. 1303–1305. [20 refs.]

MUKERJEE (S. B.). An Interesting Case of Malaria.—*Indian Med. Gaz.* 1927. July. Vol. 62. No. 7. p. 388.

RACHINA (M. G.). Index bibliographique des travaux russes sur le paludisme depuis 1922 à 1926.—*Russian Jl. Trop. Med.* 1927. Vol. 5. No. 7. [In Russian pp. 450–467.]

SCHARFF (J. W.). Notes on Practical Measures of Malaria Prevention from the Point of View of Mosquito Control.—*Malayan Med. Jl.* 1927. June. Vol. 2. No. 2. pp. 49–53.

WARASI (W.). Das Zentralnervensystem bei der Malaria tropica.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Sept. Vol. 31. No. 9. pp. 432–434. [6 refs.] [Trop. Dis. Inst., Tiflis.]

BLACKWATER FEVER.

KIKUTH (Walter). Ueber den heutigen Stand der Schwarzwasserfieberfrage mit eigenen experimentellen Beobachtungen. [**The Present Position of the Blackwater Fever Question, with Some Experimental Observations.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Nov. Vol. 31. No. 11. pp. 501–518. [63 refs.] [Inst. for Ship & Trop. Dis., Hamburg.]

This paper is, as its title implies, mainly a summary of the present state of knowledge regarding certain aspects of blackwater fever. The author defines blackwater fever as a haemolysis of sudden onset accompanied by rigors and a rise of temperature and leading to haemoglobinuria; it is to be regarded as a symptom of manifest or latent malaria and in most cases is precipitated by quinine. It is not to be confused with haemoglobinurias which are caused by a whole series of exogenetic factors such as organic or inorganic poisons, or infective processes, or with the closely similar condition known as paroxysmal haemoglobinuria.

The author refers to the records collected by STEPHENS, NOCHT, and THOMSON, showing that malaria parasites disappear from the blood in the majority of cases after the onset of the paroxysm, and he advances a theory to account for their disappearance. It is generally accepted that erythrocytes invaded by malaria parasites are destroyed, and with the destruction of the red cells the fate of the parasite is sealed. Probably the haemolysis is not accomplished directly but indirectly with the aid of the reticulo-endothelial elements. The reticulo-endothelium comprises, however, at the same time, those cells of the organism which phagocytose the malaria parasites, and in which one can often find malaria parasites after death even in those cases where the blood was negative during life. Further, it must be remembered that after the enormous destruction of red cells an intensive regenerative process sets in very quickly; this is accompanied by a considerable neutrophil leucocytosis. In other words, there is an extraordinarily intensive inflammation of the whole haemopoietic system. The organism mobilizes its entire power for the purpose. It is now generally recognized that the haemopoietic system is to a certain extent the site of immune-body formation, and consequently one may conclude that the resistance of the organism to the malaria infection is also raised and a sort of auto-immunization takes place which naturally need not be of long duration.

Reference is next made to the facts that blackwater fever is usually associated with the malignant tertian parasite and that although attacks do occur in patients who have not taken any drug, quinine in the vast majority is the exciting cause. NOCHT and his collaborators have shown that quinine assists the action of haemolytic amboceptor in the animal organism, although this is not to be seen *in vitro*. If dogs be injected intravenously with a specific haemolysin and then given quinine intravenously a marked haemolysis results, although this does not occur, or only in a modified degree, in the control animals which had received the amboceptor, but not the quinine.

The remainder of the paper consists of references to, and brief discussions of, various recent articles dealing with different problems in blackwater fever, all of which have already received notice in this *Bulletin*.

W. Yorke.

EBERT (M. K.). Zur Frage der Pathogenese der Hämoglobinurie bei der Malaria (Schwarzwasserfieber). [**The Pathogenesis of Haemoglobinuria in Malaria.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1927. Nov. 14. Vol. 53. Nos. 3-4. pp. 297–314. [14 refs.] [Educ. Commissariat, R.S.F.S.R., Moscow.]

The work described in this paper was undertaken with the object of examining the theory of KRITSCHEWSKY and MURATOFFA that the haemoglobinuria in malaria results from a combined action of quinine and the lipoids of the organism [this *Bulletin*, Vol. 21, p. 386].

The following are the conclusions :—

1. Human serum possesses the power of producing, with quinine, haemolysis of human erythrocytes.

2. As in the case of snake venom the activation of quinine haemolysis is brought about by active or inactivated (56° C.) serum.

3. Along with those substances which possess the power of activating quinine haemolysis there occur in some sera also antagonistic bodies.

4. The degree of haemolysis in the activation of the haemolytic power of quinine by lecithin depends to a certain extent on the individuality of the erythrocytes.

5. The presence of an individual factor both in the activation of the haemolytic power of snake venom by lecithin, and also in the haemolysis by cobra poison alone, is to be regarded as further proof of the analogous action of quinine and snake venom.

6. This analogy is confirmed by haemolysis experiments with the combination cobra poison+lecithin+serum as well as by haemolytic experiments on erythrocytes (after previous treatment with quinine and snake venom) with hypotonic sodium chloride solution.

W. Y.

MAYEDA (Minoru). [**Experimental and Clinical Studies on the Hemolytic Phenomena caused by Quinine Hydrochloricum, and Considerations on the Pathology of Black Water Fever.**]—*Fukuoka Ikadaigaku Zasshi* (*Jl. Fukuoka Med. Soc.*). 1926. Oct. Vol. 19. No. 10. [Summarized in *Japan Med. World.* 1927. May 15. Vol. 7. No. 5. p. 147.]

The haemolytic effect of quinine is due to a chemical action of the drug, whilst that of hypotonic saline is mechanical. Quinine haemolysis is accelerated by heat, alcohol, ether, etc. ; it is markedly inhibited by acids, but increased by alkalies. Erythrocytes which had been treated with quinine reacted quite differently from those treated with alkalis or acids. Injections of acids or alkalis had no influence on the haemolytic action of quinine *in vivo*. The author states that quinine haemolysis *in vivo* was influenced by seasonal variations and was more marked in summer than during the colder seasons. The paper concludes with a hypothesis of the genesis of blackwater fever.

W. Y.

UNITED FRUIT COMPANY, BOSTON, MASS. FIFTEENTH ANNUAL REPORT MEDICAL DEPARTMENT. 1926. pp. 47–48. [1 ref.]—**Some Notes relating to Malaria and Blackwater Fever.**

Significant observations from Banes Hospital, Cuba, of relationship between malaria and blackwater fever are recorded. The latter is confined to Old World Spaniards and " high-caste Cuban races." In malaria surveys Dr. H. C. CLARK found two cases with abundant young

subtertian forms, neither showing any ill effect. Within 6 hours one of them was down with fever and haemoglobinuria, was admitted immediately to hospital, and was then without malaria parasites detectable in blood films.

In the second case the haemoglobinuria came on 5 days after the routine blood examination, but no parasites were found on his immediate admission to hospital.

The injection, into a negro not suffering from acute disease, of 10 cc. of the whole blood of a man in his first paroxysm of haemoglobinuria resulted in no ill effects—no appearance of malaria or blackwater fever within an observation period of three weeks.

Clayton Lane.

HUDICOURT (Lélio). De la fièvre bilieuse hémoglobinurique. [**Blackwater Fever.**]—*Bull. Soc. Méd. d'Haiti.* Port-au-Prince. 1927. Apr. Year 1. No. 2. pp. 7–11.

This note gives a brief summary of the general characters of blackwater. The author states that in the course of his practice in Haiti, which extends over a period of more than 30 years, he has only encountered 8 cases of blackwater fever. All these were fatal, except the last, and all occurred amongst adult Haitians except one, who was a young Syrian.

W. Y.

AGUILAR (Ricardo). **Treatment of Haemoglobinuric Fever with the use of Haemostatic Serum Intravenously.**—*Fifteenth Ann. Rep. Med. Dept. United Fruit Company, Boston, Mass.* 1926. pp. 63–66. [1 ref.]

This report deals with the treatment of 20 cases of blackwater fever with haemostatic serum "Lapenta" (Parke, Davis & Company).

Of the 20 cases, examination of the blood showed 10 to be infected with *P. falciparum*, 3 with *P. vivax*, and 7 to be negative. The cases were of three different clinical types, i.e., 12 were acute, 5 subacute, and 3 paroxysmal. The features of the different types are described. The serum was administered intravenously in doses of from 2 to 4 cc., diluted with 20 cc. of normal saline, and given once or twice daily for the first two days. All 20 cases recovered. The rationale of the treatment is based on the belief that in haemoglobinuric fever the anti-haemolytic substance in the blood is at fault, and that the injection of normal horse serum supplies this anti-haemolytic substance and thus prevents further haemolysis.

W. Y.

MACKIE (A. S.). **Blackwater Fever: Third Attack.**—*Kenya & East African Med. Jl.* 1927. Sept. Vol. 4. No. 6. pp. 188–189.

Clinical details are given concerning an attack of blackwater fever in a Seychelles woman who had lived in Kenya for 8 years and, during this period, had suffered from two attacks of this disease. It is remarked that intravenous injections of sodium bicarbonate had "a wonderful effect in clearing the urine and in increasing its amount."

W. Y.

CIAVALDINI (J.). Un cas d'hémoglobinurie chez une paludéenne n'ayant jamais absorbé de quinine. [**Haemoglobinuria in a Malaric who had never taken Quinine.**]—*Arch. Inst. Pasteur d'Algérie.* 1927. Mar. Vol. 5. No. 1. pp. 48–50. [1 ref.]

Details are given of a case of malaria in which blackwater fever developed, although the patient had never taken quinine.

W. Y.

WEST AFRICAN MEDICAL JOURNAL. 1927. Oct. Vol. 1. No. 2. p. 15.—**The Medical Officer and the Microscope in West Africa.** [A. C.]

Dr. A. C[ONNAL], Editor in Nigeria of this promising venture in medical journalism, the *West African Medical Journal*, referring to a letter on Blackwater Fever published in the *Lancet* and reviewed in this *Bulletin*, Vol. 24, pp. 652–3, takes objection to a comment made by the reviewer on a statement by the writer of the letter to the effect that the microscope was rarely used on the West Coast. The reviewer, in Dr. Connal's judgment, should have emphatically contradicted the implied neglect. Dr. Connal says that a microscope is issued to each medical officer on his arrival, and on his departure is thoroughly overhauled before re-issue. It is not only "largely and usefully used in medical stations but is in most cases regarded as a necessary friend." With his criticisms of the statements about blackwater fever we are not now concerned, but this dictum merits quotation—"The person who blindly trusts to 'religiously' taken doses of quinine, whilst neglecting the ordinary and common-sense safeguards against mosquito-bites, is one of our greatest problems in West Africa."

A. G. B.

SHAHA (Brajaballav). A Case of Blackwater Fever.—*Calcutta Med. Jl.* 1927. Oct. Vol. 22. No. 4. pp. 190–199. [8 refs.]

TROPICAL MYCOLOGY.

PINOY (P. E.) & NANTA (A.). Sur l'existence fréquente d'une mycose de la rate en Algérie. [**On a Common Mycosis of the Spleen in Algeria.**] —*C.R. Acad. Sci.* 1927. Feb. 7. Vol. 184. No. 6. pp. 346–347.

The "cysts" found in cases of splenomegaly in which nodules of Gamna are present, are either organs of fructification, or perithecial appendages of the fungus *Sterigmatocystis nidulans*; such cases of splenomegaly being really mycetomas of the spleen. The fungus may penetrate through the skin or through the intestine, and, in doing so, may admit secondary infections of various bacteria, the nature of which may modify the clinical aspect of the condition.

P. Tate.

EMILE-WEIL (P.), GRÉGOIRE & FLANDRIN. La splénomégalie mycosique. [**Mycotic Splenomegaly.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1927. May 26. Year 43. 3rd Ser. Vol. 51. No. 17. pp. 713–717.

PINOY and NANTA in 1926 showed that many cases of chronic splenomegaly in Algeria are of mycotic origin, the parasite being *Sterigmatocystis nidulans* (see preceding summary). The present authors report that mycotic splenomegaly is also frequent in France, especially in Paris where they have found, by operation or autopsy, 7 out of 16 cases to be of mycotic origin.

Clinical diagnosis of the condition is not possible and it is mostly seen in young persons and men. Infected spleens weigh 1–2 kilogrammes, and usually contain characteristic yellowish-brown nodules about the size of a millet seed, which vary in abundance, 1–3 or less being found in a square centimetre. The nodules are filled with mycélial filaments and in several cases easily identifiable heads of an Aspergillus were seen. The fungus grows readily on Sabouraud's medium, and appears to be an Aspergillus, although NANTA and PINOY cultivated a Sterigmatocystis from their cases.

One patient operated on two years ago is cured and enjoys perfect health, but the other cases are too recent to judge as to the final results.

P. T.

GRÉGOIRE (Raymond), EMILE-WEIL (P.) & FLANDRIN (P.). Note pour servir à l'étiologie de la maladie de Banti (la splénomégalie mycosique). [**The Etiology of Banti's Disease.**]—*Bull. et Mém. Soc. Nat. de Chirurg.* 1927. May 28. Vol. 53. No. 17. pp. 734–737. [8 refs.]

This is a preliminary account of the seven cases of mycotic splenomegaly met with in Paris [see below]. None of the patients had ever left France, and none suffered from malaria or syphilis. The earliest symptom is nearly always haemorrhage of the alimentary canal, and it may precede other symptoms by several years. The spleen is very greatly enlarged and there is generally pronounced anaemia. Later, there is enlargement of the liver and ascites. In the later stages, the clinical aspect of the disease is the same as that of the third stage of Banti's disease.

P. T.

EMILE-WEIL (P.), GRÉGOIRE (Raymond) & FLANDRIN. Anatomie pathologique de la splénomégalie mycosique. [**Pathological Anatomy of Mycotic Splenomegaly.**]—*Ann. d'Anat. Path. et d'Anatome Normale.* 1927. June. Vol. 4. No. 6. pp. 587–594. With 1 text fig. & 4 coloured figs. on 1 plate. [Labs. of Clinical Surg. & of Parasit., Algiers.]

This paper is a description of the pathological anatomy of the spleens of 7 cases of mycotic splenomegaly met with in Paris [see above]. All the spleens were very much enlarged and hypertrophied, and contained more or less numerous yellowish nodules, varying in size and form. These nodules were previously described by GAMNA in cases of splenomegaly. The nodules consist of a peripheral haemorrhagic zone, and a central zone consisting of vessels with sclerotic walls, bunches of connective fibres and fibroblasts, and, towards the periphery, giant cells. Amongst these elements were various fungous structures, consisting of closely segmented hyphae and fructifications, distinct Aspergillus heads sometimes being visible. In places the fungal elements were incrusted with iron salts, or calcified.

The whole spleen is more or less sclerotic; the follicles of Morgagni are always enlarged; and there are sub-capsular or central haemorrhagic zones. There is more or less cirrhosis of the liver, with granular degeneration of the hepatic cells, but a fungus was never detected in this organ.

The fungus appeared to be the same in all cases, and cultures of an Aspergillus were readily obtained, but the species, which is not *fumigatus*, has not been identified. Bacterial infection of the spleen was not recognized in sections or by culture.

P. T.

EMILE-WEIL (P.), CHEVALLIER (P.) & FLANDRIN (P.). Le diagnostic des splénomégalies mycosiques par les moyens de laboratoire. [**Laboratory Diagnosis of Mycotic Splenomegaly.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1927. Nov. 3. Year 43. 3rd Ser. Vol. 51. No. 30. pp. 1425–1429.

Cuti- and intradermo-reactions with Aspergillus were not successful. Sero-agglutination with Aspergillus was also unsuccessful, but the fixation reaction gave promising results. For the fixation reactions two antigens were used from two strains of an Aspergillus (*A. amstelodami*) cultivated from infected spleens. Cultures several months old gave better antigens than newly isolated cultures. A positive reaction is not specific for mycotic splenomegaly, but is nevertheless of some confirmatory value. A negative reaction does not rule out a diagnosis of mycotic splenomegaly. In cases of mycotic splenomegaly the reaction remained positive after the removal of the spleens; and in some cases the reaction was at first negative and became positive after removal of the spleen. Positive reactions may be given by myeloid leucaemia, Hodgkin's splenomegaly, leprosy, certain cases of suppurating bubos, sometimes in secondary or tertiary cases of syphilis, and occasionally in cutaneous tuberculosis, and in some cases of ulcers of the legs.

P. T.

NANTA (A.). Une mycose splénique. Etude histologique. [**Histology of Splenic Mycosis.**]—*Ann. d'Anat. Path. et d'Anatomie Normale.* 1927. June. Vol. 4. No. 6. pp. 573–585. With 3 text figs. & 3 coloured figs. on 1 plate. [1 ref.] [Labs. of Clinical Surg. & of Parasit., Algiers.]

Twenty extirpated spleens were studied, of which 3 were removed for injury to the spleen, one for a hydatid cyst, one for malarial hypertrophy, and the remaining 15 for "splenic anaemia." The last formed two groups: one in which only bacteria were found and no nodular lesions were present; and the other in which, in addition to the bacteria, a fungus and nodular lesions were present. The clinical aspect of both groups was similar.

The nature of the lesions in the last group varies with the duration of the disease. The chief types of lesions are sclerotic pigmented nodules, and lesions in the pulp. The nodules vary in size from that of a pin's head to 2–3 mm. in diameter, and are yellow in colour. Sometimes they are extremely numerous, but may be very small and scarce in other cases. The nodules show three zones: a peripheral haemorrhagic zone; a sclerotic fibroid zone; and a central zone formed of bundles of hyaline, basophilous elements. Small calcified corpuscles of varying sizes are present in the nodules, and are composed of calcified fragments of hyphae, Aspergillus fructifications, and abortive perithecia. These are sometimes impregnated with iron salts. Calcareous and ferrugineous corpuscles arranged in concentric zones are also present. Streptococci and Spirilla are frequently present. Similar nodules have been described by GAMNA and others, without the presence of parasites having been noted, so that it is doubtful if the nodules are specific to the mycotic infection. From three of the cases cultures of a Sterigmatocystis were obtained.

The lesions in the pulp consist of sclerosis of the vessels and cellular proliferation and infiltration. Occasionally, other types of lesions were present in the spleen and the liver was enlarged, congested and with moderate sclerosis, while in one case the ganglia of the splenic hilus were infected.

The frequent association of mycotic and bacterial infections makes it difficult to decide the part played by each in the development of the lesions, and whether the mycotic infection is primary or secondary.

P. T.

SCHWEIZER (A.). Ueber ägyptische Splenomegalie. [**Egyptian Splenomegaly.**]—*Schweiz. Med. Woch.* 1927. Oct. 22. Vol. 57. No. 43. pp. 1017–1027. With 7 text figs. [19 refs.] [Path. Inst. Univ., Geneva.]

The author investigated the extirpated spleens of five cases of "Egyptian Splenomegaly," two of which terminated fatally. In one of the fatal cases there were pulmonary complications, and in the other complications of infiltration of the liver and the formation of pseudo-tubercular nodules owing to the presence of eggs of *Schistosoma mansoni.* Full clinical details of all the cases, both before and after operation, are given; and the pathological anatomy of the spleens is described in detail. In three of the cases the spleens contained fibrous granules containing fungous hyphae, which were frequently

enclosed in giant cells, and from which swollen and segmented hyphae often extended into the surrounding tissue. In no case were other parasitic elements found in the spleens.

The granules are formed of connective tissue, and have, usually, one large and two small arteries running in them. Part of the connective tissue of which they are formed, portions of the walls of the arteries, and all the hyphae give a strong iron reaction with ammonium sulphide and with Turnbull's reagent. The granules are the only part of the spleen which give these reactions. The only effective treatment is splenectomy ; but this is unavailing when ascites has developed, and such cases always terminate fatally.

The author concludes that some cases of Egyptian splenomegaly must be placed in the new group " Splenomegaly mycotica," which WEIL created for certain cases of Algerian splenomegaly found by him to be of fungus origin. [See above.]

P. T.

REVIEWS AND NOTICES.

HEGNER (Robert). [Ph.D., Professor of Protozoology in the School of Hygiene and Public Health of the Johns Hopkins University.] **Host-Parasite Relations between Man and his Intestinal Protozoa.** [The Century Biological Series, Robert Hegner, Editor.]—pp. xiii+231. With 21 figs. (2 plates). 1927. London: New York. The Century Co. [15s.]

In the organization of protozoological work in a school of hygiene and public health the author was at once struck by the lack of co-ordination between medical and zoological phases of the subject and between these and methods of prevention and control. In order to overcome this difficulty in connexion with the intestinal Protozoa of man the author has produced this book, divided into five chapters, in which is gathered together from many scattered sources all the important information regarding the relation of these parasites to their hosts.

In introducing the subject in Chapter I a parallel is drawn between a free-living and a parasitic amoeba, and it is shown that in morphology and in every process and activity that occurs during the life-cycles there are no essential differences. A brief enumeration of the intestinal Protozoa of man is followed by a general account of the biology of Host-Parasite Relations between man and his intestinal Protozoa, including such subjects as the epidemiology of transmission, clinical and parasitological periods during the course of a natural infection, distribution and localization of parasites within the host, passive resistance of the parasite, the parasite's method of attack, changes in the host caused by the parasite, changes in the parasite due to residence in the host, host-parasite adjustments during an infection, therapeutics, route taken by parasites in escaping from the host. The next general section deals with Host-Parasite Specificity in which are considered host susceptibility, parasite infectivity, some problems in host-parasite specificity among intestinal Protozoa. Finally, certain problems in host-parasite relations among intestinal Protozoa are dealt with and a programme of subjects which might with advantage be investigated by a group of protozoologists variously trained in zoology, medicine and public health, is given.

In Chapters II to V, occupying about three-quarters of the text, the various intestinal Protozoa are dealt with individually. Their morphology and life histories are briefly described, and any knowledge which has been gained, and which falls under the above and other headings, is carefully reviewed and discussed in its bearing on public health in its widest application. In addition to purely human parasites the allied forms in animals are considered, for it is not clear in all cases that these may not parasitize man. The author has been careful to give exact references so that original papers may be found in the list of literature at the end of the book, where also are added an author and a subject index. All those interested in the question of prevention of disease will benefit by the perusal of this interesting book, which will afford them a rational and scientific basis for any action they may take. The book is light and of convenient size. It is printed on thick paper with clear, easily readable type, and is illustrated with black and white drawings of the organisms discussed. It could be read with profit by any student of medical protozoology.

C. M. Wenyon.

STITT (E. R.) [A.B., Ph.G., M.D., Sc.D., LL.D., etc.]. **Practical Bacteriology, Blood Work and Animal Parasitology including Bacteriological Keys, Zoological Tables and Explanatory Clinical Notes. A Compendium for Internists.** Eighth Edition, Revised and Enlarged.—pp. xv+837. With 1 plate & 211 other illustrations containing 683 figs. 1927. London: H. K. Lewis & Co. Ltd. [24s.]

The appearance of a new edition of this extremely handy book is a welcome event; it is, in fact, an enlargement of the seventh which was reviewed in this *Bulletin* in 1923. In endeavouring to reduce the size of the volume, by extensive use of small type, by one hundred pages, the author has had to acknowledge failure and, in view of the important additions to our knowledge of clinical pathology in the past four years, has been faced by the necessity of enlarging by more than that number of pages over the seventh edition.

The increasing importance of dental pathology and its bearing on many diseases have made it necessary to include a new chapter on the diagnosis of infections of the teeth.

Other additions include the Kahn test, owing to its relative simplicity and high specificity, the adoption of new nomenclature in the bacteriological keys, and sections describing recent advances in the Streptococcus groups have to be specially noted.

Part II.—"The Study of the Blood"—contains some of the most important changes with sections on blood grouping and compatibility.

In the Appendix new sections on liver and kidney function tests have been added.

The mass of information included in these eight hundred pages exceeds that of any other medical volume of its size, and for every laboratory worker, both within the tropics and without, Stitt's handbook remains indispensable. It must be admitted that the illustrations still remain the weak feature of the book.

Philip Manson-Bahr.

LOTSY (G. O.). [Member of the "Institut d'Egypte," Cairo.] **The Radiographic Diagnosis of Bilharziasis.**—In English 30 pp. With 11 photographic plates (43 radiographs, 1 photograph) 11 plates with 42 schemes and 2 schemes in the text. [Also in French and Arabic.] 1927. Cairo: H. Friedrich & Co., Booksellers & Publishers. Printed by the Amalgamated Press, Egypt.

This records, in English, French and Arabic, an interesting series of observations made of the changes produced in the tissues, chiefly in the urinary system, of persons suffering from bilharziasis, as made evident by means of X-ray examination.

The text of each of the three linguistic sections opens with a note of "parasitic, anatomical and clinical facts." In the course of this it is pointed out that quantities of eggs of the Bilharz worm, in their effort to penetrate through the walls of the viscera, remain in the various layers of the bladder, ureters and intestine. After a time, usually a year, these eggs have become calcified and collectively produce shadows recognizable on skiagraphs of the affected parts, the observation and interpretation of such shadows forming the subject matter of this study.

The second, radiographic, part of each section describes a number of illustrative cases with reference to photographic reproductions included in the final section of the book.

This method of presentation is open to adverse criticism on general grounds but the author has made a careful selection of cases, and the reproductions of skiagraphic appearances are so excellent that each point

brought out in the text is convincingly demonstrated. A minor point has escaped attention in the reproductions, namely the advantage of indicating on each skiagraph the orientation of the patient. A simple R or L imprinted on the appropriate margin of the picture would obviate repeated cross reference to the diagrams or to the text. The diagrams referred to are set out opposite each plate of skiagraphic reproductions and should help the uninitiated to appreciate the variations in shadow density upon which depends the radiologist's interpretation.

The effect of infiltration of the bladder wall with calcified ova is the production of a definite outline shadow of the bladder, and similarly with the ureters. The appearance of such abnormal shadows and their variations are described and a final section then deals with "differential diagnosis," a dangerous term to employ in connexion with any single method of examination. The necessity for correlation with other observations is not, however, overlooked and confirmation by cystoscopy is referred to. Urinary calculus is the condition most likely to cause confusion in a skiagraph and the differential points are well brought out, especially in several cases in which the two conditions are co-existent. This work should be of considerable value to the clinician; certainly to the radiologist it presents a most interesting record of observations which must be of the highest value to any one likely to meet with such cases in his practice.

John Muir.

SCHILLING (Cl.). Immunität bei Protozoeninfektionen. [**Immunity in Protozoal Infection.**]—*Handbuch der pathogenen Mikroorganismen.* 1927. Vol. 8. No. 9. pp. 95–140. With 1 text fig.

The author introduces his subject by explaining why it is that knowledge of immunology in protozoal diseases is less advanced than in the case of bacterial infections. In many cases Protozoa can be studied only in the natural human or animal host and when they can be transferred to laboratory animals they may become profoundly changed in character. Only a comparatively small number can be cultivated and not infrequently the cultural forms differ from those which are actually parasitic. The natural methods of transmission are not easily carried out, while involved life histories tend further to complicate the investigations. Nevertheless, considerable progress has been made and with few omissions the subject is clearly dealt with in the paper under review.

There is a general section of 25 pages followed by a special section dealing with certain individual organisms of 17 pages. Four and a half pages of the more important references (prior to 1927) are given. Though it is admitted that the spirochaetes are not Protozoa they are included, as in many respects they behave serologically in a similar manner. Under the heading of immunity of normal animals and man the resistance of animals to inoculation with human malarial parasites is mentioned and with this is contrasted the susceptibility of laboratory animals to pathogenic trypanosomes and spirochaetes. The statement that *Entamoeba histolytica* appears to be specific to man is hardly correct in view of the ease with which strains can be maintained in kittens, if not in monkeys. The greater part of the general section is devoted to a consideration of immunity in uninfluenced infections. The separation of parasites, particularly trypanosomes, as distinct species merely because of serological differences is not favoured by the author. The term paroxysmal toxin is introduced for such cases as malaria where the liberation of this substance occurs with a definite suddenness. In malaria at least it appears that the paroxysmal toxin has no appreciable action as an antigen. The subject of infections which terminate in death or recovery is discussed, as also those which are characterized by definite relapses. The serological relationship of the first attack and relapse strains receives attention and this is followed by a consideration of reaction products other than antibodies. Such are precipitin, agglomeration,

attachment, platelet fixation (adhesion phenomenon), trypanolysin, auto-agglutination of red cells, action of human serum, opsinin, complement fixation. The bulk of the work under these headings has to do with trypanosome infections. It is perhaps unfortunate that the complement fixation test of WATSON for the diagnosis of dourine in Canada receives no mention as it appears to be the one instance in which a practical application has been obtained.

The difficult question of the disappearance of symptoms quite apart from the termination of infection is carefully discussed. Under this heading malaria and piroplasmosis are dealt with. Such persisting infections after apparent recovery have been described under various names apart from the author's term labile infections, viz., tolerance, dumb infections, infectious immunity, premunition. The important work of SERGENT and his co-workers, who introduced the term premunition in piroplasmosis, is barely mentioned. The relation of these labile infections to superinfections and relapse infections is next discussed, while the important subject of the localization of parasites in special organs, as, for instance, spirochaetes in the brain, is considered. It is concluded that the action of induced malaria in the treatment of paralytics is probably due to injury to the walls of the blood vessels permitting the passage of antibodies into the brain substance. The immunity which follows administration of chemical agents and that resulting from injection of killed parasites terminate the matter dealt with in the general section.

The special section deals with individual infections which are described as those which result in immunity after a single attack (East Coast fever, chicken spirochaetosis, yellow fever, Weil's disease, rat trypanosomiasis, yaws, leishmaniasis), those which result in immunity after more than one attack (relapsing fever), those which rarely produce immunity (malaria, piroplasmosis) and those which do not give rise to a sterilizing immunity (Texas fever of cattle, the allied disease of sheep, trypanosomiasis, amoebic dysentery). Finally, the toxic substances isolated from spores of sarcosporidia are discussed. Most of the important data relating to the above mentioned infections are included but the author is careful to point out that as this article is merely part of a general handbook further details will be found in the sections devoted to the diseases themselves. This may account for the failure to mention the important work of TALIAFERRO on the reproduction-inhibiting substances which appear in the blood of rats infected with *Trypanosoma lewisi*. In connexion with yellow fever Noguchi's spirochaete is erroneously referred to as *Leptospira icterogenes* which is the name employed in Germany for the organism of Weil's disease. In connexion with kala azar it is stated that the disease in India is probably always fatal, though authorities have undoubtedly come to the conclusion that the number of spontaneous recoveries is not inconsiderable. Further some will not accept the author's statement that up to the present no single case of spontaneous recovery from sleeping sickness has been reported.

Apart from these and a few other doubtful points the article undoubtedly gives a very comprehensive and accurate review of a difficult subject. It contains a vast amount of information condensed into a small space and, being merely one of a series of articles in the well known handbook of pathogenic micro-organisms, it fulfils its function in a very satisfactory manner and can be accepted as a reliable survey of the present position of immunity in protozoal infections.

C. M. Wenyon.